Arizona Medicine

Journal of

ARIZONA MEDICAL ASSOCIATION

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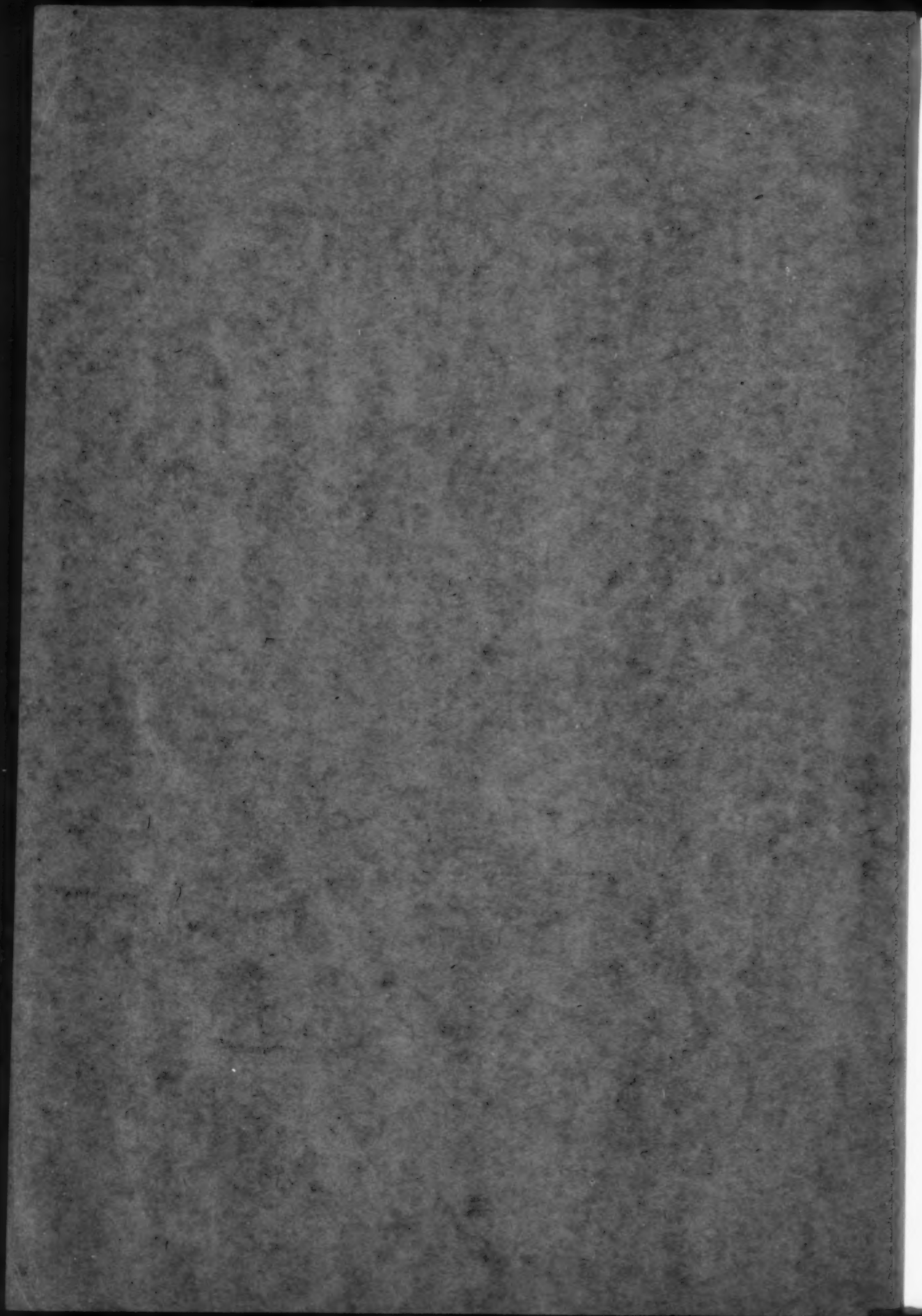
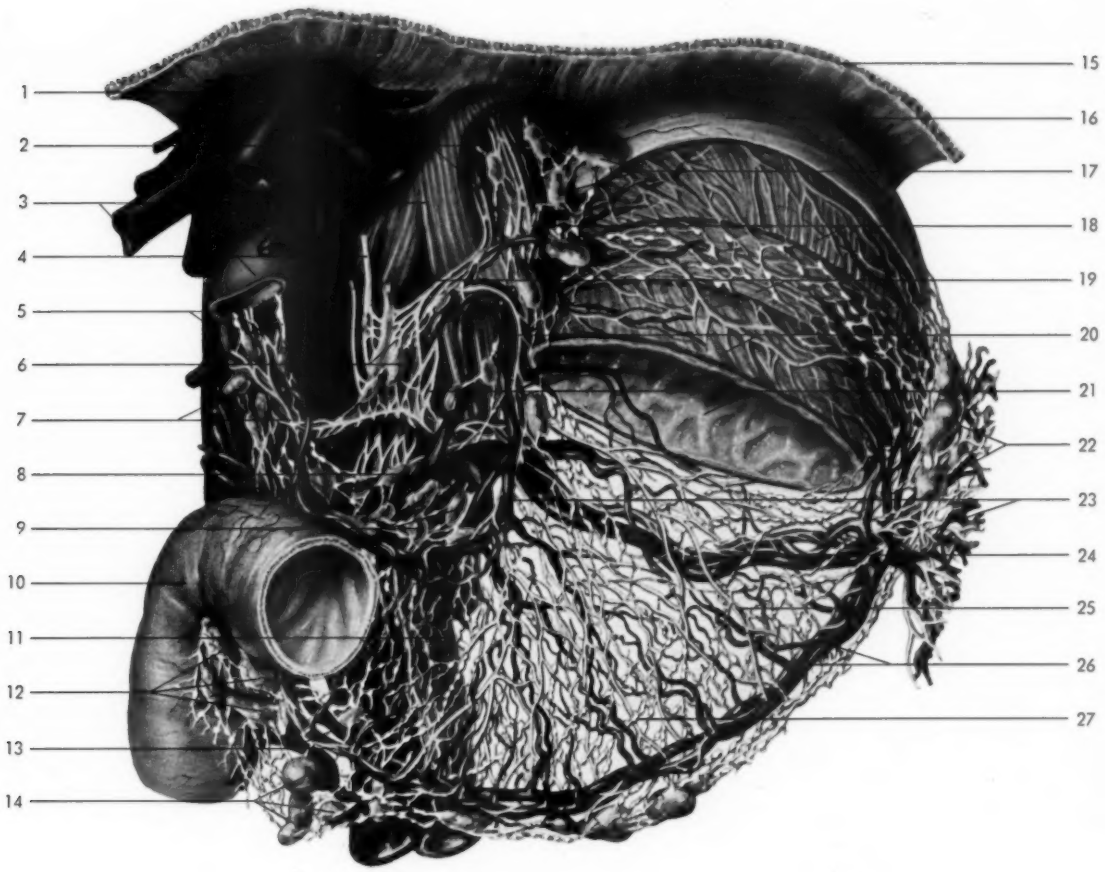


Anatomy *of the* Stomach



1 Middle and left hepatic veins

2 Right vagus nerve and esophagus

3 Right hepatic vein and crura of diaphragm

4 Inferior vena cava and greater splanchnic nerve

5 Portal vein and hepatic artery

6 Celiac plexus and celiac artery

7 Hepatic lymph node and hepatic rami of vagus nerve

8 Gastroduodenal artery and suprapyloric lymph nodes

9 Superior gastric lymph nodes

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11 Superior mesenteric artery and vein

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13 Right gastroepiploic artery and vein

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15 Diaphragm

16 Serosa

17 Paracardial lymph nodes

18 Left vagus nerve and longitudinal muscular layer

19 Abdominal aorta and circular muscular layer

20 Left gastric artery and oblique muscular layer

21 Celiac rami of vagus nerve and gastric mucosa

22 Splenic lymph nodes

23 Left gastric (coronary) vein and splenic rami of vagus nerve

24 Splenic artery and vein

25 Gastric rami of vagus nerve

26 Left gastroepiploic artery and vein

27 Gastric lymphatic plexus

This is one of a series of paintings for Lederle by Paul Peck, illustrating the anatomy of various organs and tissues of the body which are frequently attacked by infection, where aureomycin may prove useful.

Lederle

ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

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Published monthly by the Arizona Medical Association. Business office at 426 Heard Building, Phoenix, Arizona. Subscription $3.00 a year, single copy 25c. Entered as second class matter March 1, 1921, at Postoffice at Phoenix, Arizona, Act of March 3, 1879.

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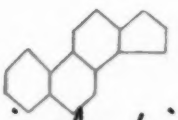
the symbol SCHERING denotes leadership in steroid hormone  research and manufacture -- including Cortogen in the most useful clinical forms. For systemic therapy, use Cortogen tablets SCHERING or injection . For eye  disorders use Cortogen ophthalmic suspension -- sterile  . The Schering seal SCHERING appears on each tablet and package -- your assurance of quality.

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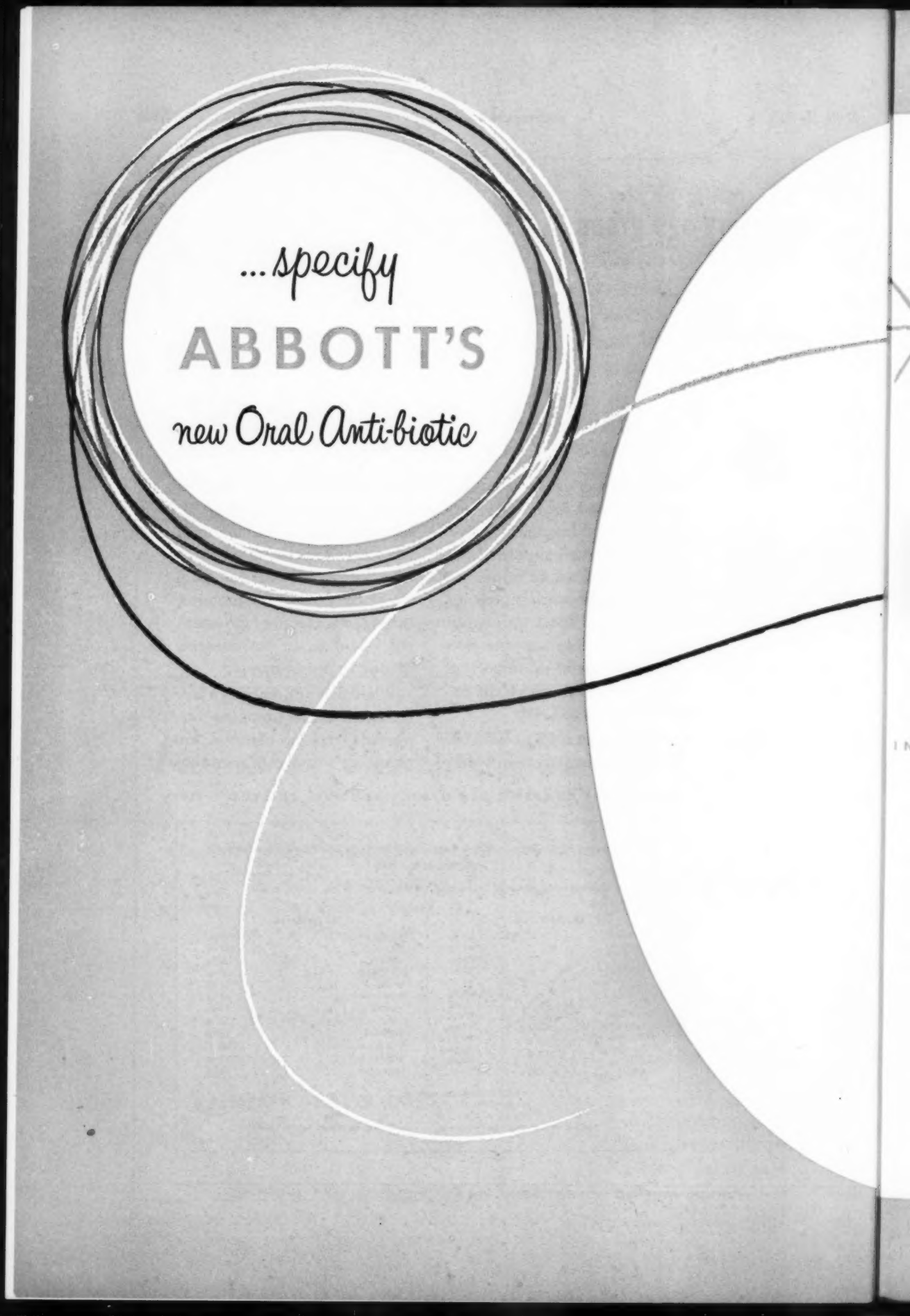
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Abbott

1. McGuire et al. (1952), J. Antibiotics & Chemo., 2:281, June.
2. Heilman et al. (1952), Proc. Staff Meet. Mayo Clin., 27:385, July 16.
3. Haight and Finland (1952), New Eng. J. Med., 247:227, Aug. 14.

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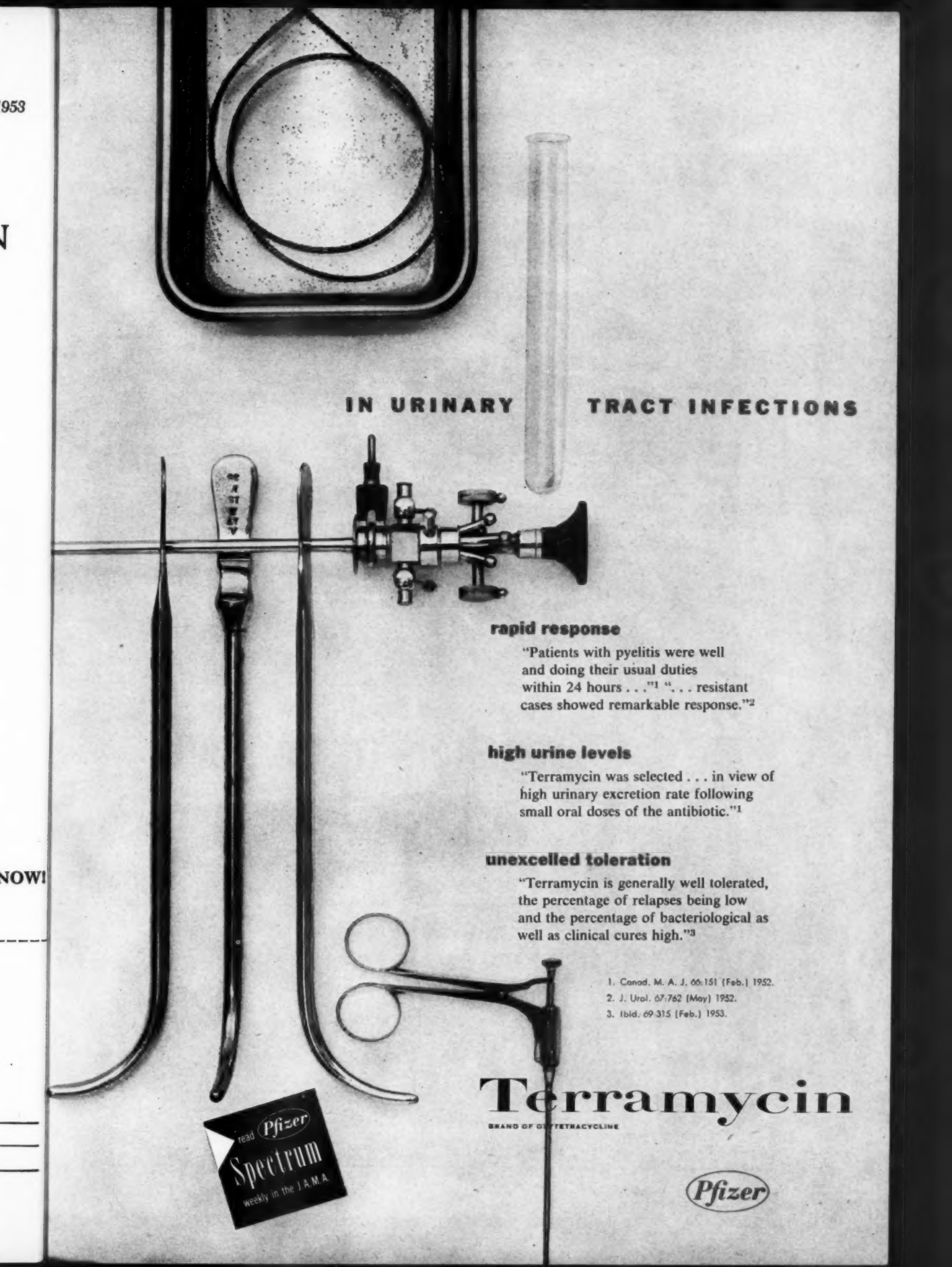
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1. Canad. M. A. J. 66:151 (Feb.) 1952.
2. J. Urol. 67:762 (May) 1952.
3. Ibid. 69:315 (Feb.) 1953.
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ARIZONA MEDICINE
Journal of Arizona Medical Association

VOL. 10, NO. 5 MAY, 1953

Original ARTICLES

CHRONIC GASTRITIS

Marcy L. Sussman, M.D.
Phoenix, Arizona
Benjamin Copleman, M.D.
Perth Amboy, New Jersey

Introduction

The diagnosis of chronic gastritis ordinarily is suggested first by the radiologist. His impression is based upon the finding of thick, fairly rigid mucosal folds often with a disturbance in peristalsis. To the radiologist with experience in the disease, the pattern is fairly characteristic. In general, however, the changes even when marked are not pathognomonic. The possibilities which must be considered are cancer, lymphoma, syphilis, gastritis and normal stomach. The differential diagnosis may require gastroscopy, exploration and/or resection.

The need for this sequence of confirmatory procedures is not unique to chronic gastritis but is often required in other gastric diseases. Chronic gastritis is unusual, however, in that there is no general agreement as to whether there is a specific symptomatology. Indeed, the disease is said by some (20) to be of little clinical significance. It is generally admitted that there is no constant correlation between roentgen, gastroscopic and pathologic findings.

In this report, we shall present cases that we consider to be examples of chronic gastritis with especial reference to their X-ray findings and their clinical course. In these individuals, we were not able to find any alternative explanation for the gastro-intestinal symptoms.

Radiologic Features

It must first be emphasized that there is no constant and precise mucosal pattern which characterizes all normal stomachs. The size, shape, direction and thickness of the folds vary from individual to individual, and even in the same patient from time to time. There is usually a general similarity of pattern under similar conditions in the same person but the occasional misinterpretation of normal variations must be anticipated.

Generally normal folds are freely flexible and are easily obliterated under manual manipulation or by the compression cone. The form, width, and numbr of folds depend on many factors. Forssell (4) believes that the volume of the relief pattern depends on the inflowing and outflowing fluids in the submucosa due to local variations in the filling of the vessels and tissue spaces. Templeton (17) believes that turgescence alone does not play a significant role in the variations of the folds in the normal stomach, but that it is important in the pathologic states. Forssell showed that the muscularis propria, and not the muscle coats of the stomach, was the chief factor in producing the motion and form of the pattern. The thickness of the mucosa itself plays a minor role in the alteration of the folds except in the rare case (see Case 4).

Any disease which affects the submucosa will alter the appearance of the mucosal pattern. Included, therefore, are submucosal infiltrating cancer, the lymphomas, and the more severe nonspecific inflamatory conditions called gastritis. In these diseases there is an increase in the cellular and fluid content of the submucosa with more

Presented at the Annual Meeting, Arizona Medical Association, 1952.

or less fixation of the mucous membrane to the muscle layers resulting in more prominent folds with loss of pliability. Generally, however, the rigidity produced by neoplasm is more marked than by other conditions.

The enlargement of the folds may be generalized or may be localized and confined to the antrum, the greater curvature, or to the fundus. The more frequent localization is in the antrum. The mucosal folds cannot be obliterated by pressure, either manually or with the use of the use of the compression cone. The enlargement and rigidity of the folds may be slight so that their caliber is only slightly above normal, and they do not quite fade out with pressure. This minimal change may not be detected even by the most experienced examiner. When enlargement of the folds and rigidity are marked, the folds may show as defects even with the stomach filled. These cases frequently show a small amount of secretions in the stomach before the examination is begun.

In gastritis, as Windholz (19) and others have pointed out, the folds have sharp borders and their course remains unchanged even in the vicinity of the most marked changes. There is ordinarily no abrupt change as in carcinoma. The abnormal folds course in the same direction as the normal folds, a fact which Berg (2) considers to be important in the differential diagnosis from carcinoma.

One helpful sign in the differential diagnosis is the demonstration of an identation into the base of the duodenal bulb when it is due to hypertrophy of the pyloric muscle. Golden (5) corroborates in his own material the statement of Serck-Hansen (15) that gastritis is invariably present with hypertrophy of the pyloric muscle. Peristalsis is apt to be irregular with localized spastic contractions which are not altered by antispasmotics and are often found unchanged on repeated re-examinations.

CASE REPORTS—GENERALIZED THICK FOLDS

Case 1. *J. E. MSH* 516443

This 50 year old white male was admitted to the Mount Sinai Hospital, New York, on Feb. 9, 1944, stating that he had been well until one month before admission. At that time he began to develop a sense of fullness and bloating in his abdomen. He had pain under his left costal margin and belched frequently. Although these symptoms were somewhat relieved by food, they were constantly present. He has been constipated since the onset of his illness. A loss of 10 lbs., in weight was attributed to restrictions in his diet.

On examination, it was noted that he swallowed air and belched constantly. The liver edge was palaple 2 fingers breadth below the costal margin. Gastric analysis showed 15 cc. of residual secretions. There were 15 units of free HC1 and 65 units of total acid after histamine. The blood count was normal. The stool guaiac test was negative. The blood Wassermann examination was negative.

A small para-esophageal hiatus hernia was found roentgenologically. A small amount of secretion was present in the stomach. There was a deformity of the antrum with marked exaggeration and irregularity of the mucosal folds. There was no evidence of mucosal destruction. The pylorus was elongated and the base of the duodenal bulb was indented. There was no delay in gastric emptying.

Gastrosocopically, the mucosa of the body was found red and covered with an excess of clear mucus. The rugae were thickened to about three times normal. The folds were grossly nodular. Those on the posterior wall were trans-segmented. Two small fresh hemorrhagic areas were seen. The folds in the antrum were also markedly exaggerated. The entire antrum was irritable with active duodenal regurgitation. The mucosa in the antrum was edematous and smooth. The impression was hypertrophic gastritis.

It was decided to have this patient return in one month for re-examination.

He was re-admitted on April 17, 1944. His gastro-intestinal complaints had disappeared with an adjustment in his diet and the omission of 10 cups of coffee and 2½ packs of cigarettes daily. The liver margin was 1 finger's breadth below the costal margin. The stool guaiac test was negative. The gastric analysis was normal. All laboratory studies were normal. The roentgenologic and gastroscopic appearances were unchanged. He was discharged with a diagnosis of hypertrophic gastritis.

The deep indention into the base of the duodenal bulb and the uniformity of the enlargement of the folds throughout the stomach were consistent with a diagnosis of gastritis.

Comment

The presence of large gastric folds, is not, in every case, an expression of gastritis. The thickness of the folds depends, as has already been stated, on such factors as the tonus of the muscu-

laris mucosae, the thickness of the submucosa and in particular, upon the tonicity of the muscularis propriae. An empty stomach may show apparently large folds. With slight distention these are smoothed out and can then be recognized as normal. The gastroscopic appearance results from the superficial appearance of the mucosa, and, as Templeton states, does not depend necessarily on the condition of the deeper structures. It is possible, therefore, that despite a normal gastroscopic appearance, large folds which are not obliterated by pressure may be due to gastritis which is mainly interstitial in character and the surface manifestations of abnormality are not recognized gastroscopically.

Case 2. *M. K. MSH* 506903

This 49 year old white man was admitted complaining of dull constant epigastric pain which was completely relieved by food, severe anorexia, and weight loss of 40 lbs. These symptoms had been present for one year. The pain was often associated with nausea and vomiting. He gave a history of suffering from a duodenal ulcer 15 years before which had healed by diet. This patient has been a known cardiac for many years but has never been decompensated.

He looked thin and chronically ill. There were systolic and diastolic murmurs at the apex. The heart was enlarged. The liver margin was 1 finger's breadth below the costal margin. His blood pressure was 108/60. There were no masses nor tenderness in the abdomen. The gastric analysis showd no free acid. His hemoglobin was 60%. The ECG was consistent with the clinical diagnosis of mitral valvular disease. The other laboratory studies were normal.

Roentgenologically, there was an irregular filling defect on the greater curvature aspect of the posterior wall of the upper half of the stomach (Fig. 1). The rugae were markedly exaggerated in the lower half. The antral portion of the stomach also showed some rigidity of the mucosal pattern, and a patulous pylorus. The roentgen diagnosis was carcinoma and it was considered likely that there was neoplastic involvement of the entire stomach. At the operation 3 weeks later the stomach was found to normal in appearance. The interior of the stomach showed a normal mucosa.

About 3 weeks after the operation, the roenegenologic examination was repeated and showed no change from the first appearance. The patient refused gastroscopy and was signed out against advice.

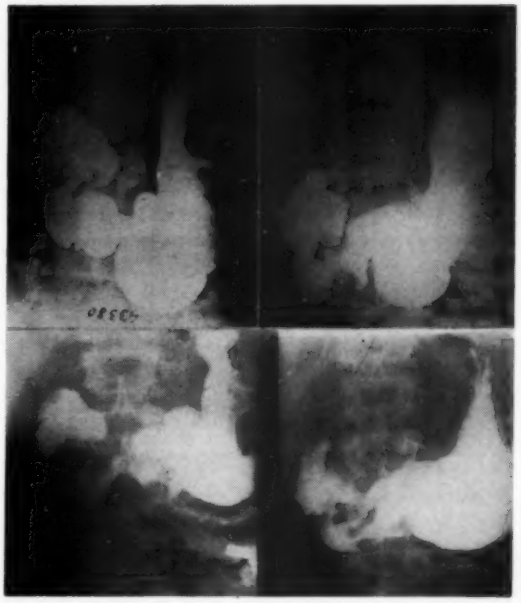

Fig. 1. *Case* 2.

a) There is an irregular filling defect on the greater curvature aspect of the upper half of the stomach, and the rugae were exaggerated in the lower half. This appearance was thought to be due to an extensive cancer. The pyloric canal was patulous. At operation three weeks later the stomach was normal.

(b) On March 15, 1944 a re-examination showed the process in the stomach to have increased in degree and extent. Gastroscopic examination showed the mucosa to be normal.

He was re-admitted on March 11, 1944. He had been well until 2 weeks before admission when he developed right upper quadrant pain 2 hours after meals. This pain was not relieved by food and was associated with nausea and vomiting. Presystolic and systolic apical murmurs present. The epigastric incision was well healed. His hemoglobin was 66% and his red corpuscles 4,100,000 per cu. mm. of blood. The stool guaiac test was negative. Gastroscopy performed on March 13, 1944 showed the fundal mucosa to be orange-red and smooth. The rugae were markedly exaggerated and prominent even after the stomach was completely distended. The pre-pyloric and antral folds were prominent. Reverse peristalsis could be seen. The gastroscopist's impression was irritable spastic stomach with nor-

mal mucosa. Roentgenologic examination on March 15, 1944 showed the antral deformity to be more marked than in 1943. The defect, it was felt, could be accounted for by the marked hyperplasia of the antral mucosa perhaps with ulcer. There was a considerable gastric residue at 6 hours. In view of the previous exploration and since the lesion had progressed only moderately in the past year, it was thought likely that hypertrophic antritis was present, probably on the basis of ulcer. The patient's symptoms disappeared during his hospital stay.

Comment

Usually, in gastritis the involvement of the mucosa and submucosa is not limited to the stomach but extends also to the duodenum. The finding therefore, of large coarse folds in the duodenum is a strong indication that the large folds in the stomach may be due to gastritis. Lymphosarcoma is the only other disease that is likely to cross the pylorus. Because this man was in at least potential cardiac failure, the mucosal alterations might have been due to this cause but the course of the disease makes its remote possibility. The presence of secretions, if pyloric obstruction can be excluded, is also significant.

Case 3

The patient, a 25 year old colored male, states that he began to vomit almost immediately after meals about 1½ years ago. There was no hematemesis. He soon began to have pain about 30 minutes after meals. The pain was griping in character, and was localized to the epigastrium. It came on at night occasionally. The pain was relieved by food, milk, or soda. Because a gastrointestinal examination was reported as normal on July 14, 1944, he was returned to duty. On October 14, 1944 the pain and vomiting became so severe that he had to be hospitalized. Another gastro-intestinal examination showed the folds of the stomach to be enlarged and rigid. No ulceration could be seen. The duodenal folds were also enlarged. The diagnosis was chronic hypertrophic gastro-duodenitis. He was much improved by diet. Gastroscopy showed a large amount of free fluid to be present. Because of the poor cooperation of the patient, and the presence of the fluid, only an occasional glimpse of the mucosa could be had. This showed the mucosa to be hyperemic and the folds to be considerably enlarged.

Comment

Involvement of the stomach and duodenum together is by no means confined to gastritis. Martin (10) found that in 15% of his cases of lymphoblastoma of the gastrointestinal tract the disease had involved the gastric and pyloric sides of the pyloric valve. In 75% of the cases where the lymphoma involved the lower end of the stomach, the duodenum was also involved. Martin was unable to make a differential diagnosis from gastritis. At operation, however, the cases of gastritis showed a reddened inflamed mucosa, while those of lymphoblastoma were a dirty gray in color. In 70% of the cases the pathologist described the rugae as being thickened and distorted. In half of these the distortion was so great that the rugae resembled cerebral convolutions.

Weber, Kirklin and Pugh (18) in an article reviewing their cases of lymphoblastoma primary in the gastro-intestinal tract, state that they have no suggestions as to how to distinguish lymphoblastoma roentgenologically from other types of neoplastic lesions.

In syphilis, the most comon pathological finding is a granulomatous pliable induration of the gastric wall (11). The pliability is due to the fact that the induration is largely marked edema of the submucosa, which is thickened out of all proportion to that of the other layers of the gastric wall. Fibrosis is also a prominent feature. Moore and Aurelius (13) state that in 70% of their cases, the lesion was prepyloric, median or hour-glass in 22%, and in 8% diffuse. The latter group simulated scirrhous carcinoma even to the extent of presenting a patulous pylorus. Meyer and Singer (12) state that the striking disparity between the roentgenologic and the palpatory size serves to distinguish this lesion from cancer. Cancer is usually more extensive than the roentgenologic examination indicates, while in syphilis there may be a surprising lack or even absence of findings compared to the roentgenologic evidence.

The association of a tumor mass with generalized thickening of the gastric folds is uncommon. Such findings are probably most common with lymphoma, but may also be simulated by polyposis of the stomach. Rarely, it may be found in hypertrophic gastritis.

Case 4

This 32 year old white male first began to complain of discomfort and epigastric pain coming at irregular intervals and relieved by alkaline powders in May 1941. His symptoms subsided during the following six months and he was sent over-

seas in December 1941. In April 1942 he noticed a return of his discomfort. He also began to have nausea and vomiting at this time. He was admitted to a hospital in June 1942, at which time an examination of his stomach demonstrated a tumor mass in the fundus. He was transferred to the hospital in November 1942, and the diagnosis of a gastric tumor was confirmed. The mass was sharply circumscribed, smooth, and the size of a lemon. There was marked thickening of the mucosa of the remainder of the stomach (Fig. 2). Because of the age of the patient the appearance was thought to be due to a lymphoma. The possibility of a leiomyoma also was suggested. The gastric analysis revealed no free HC1 and a low total acid. These findings were confirmed by repeated examinations. The patient was explored and the tumor mass and the thick rugae found. Because the surgeon felt that the mass was adherent posteriorly, only a biopsy was done. The report on this specimin was summarized as "chronic inflammation." He was observed for several months, during which time the appearance of the stomach was virtually unchanged, and then transferred to Walter Reed General Hospital. There the laboratory and roentgenologic findings were confirmed. A diagnosis of lymphoma or leiomyoma was also made. The patient was subjected to subtotal gastrectomy and esophago-gastrostomy, but died on the fifth-postoperative day.

The final diagnosis was chronic hypertrophic gastritis with tumor formation due to localized swelling of the mucosa and submucosa. This case has been reported in detail by Hinkel (7).

Comment

The stomach in somewhat similar cases described by Freedman, Glenn and Laipply (3) were increased in size and consistency, had unusually thick walls and cut with increased resistance. They state that "by gross examination alone it was difficult to exclude diffusely infiltrat-

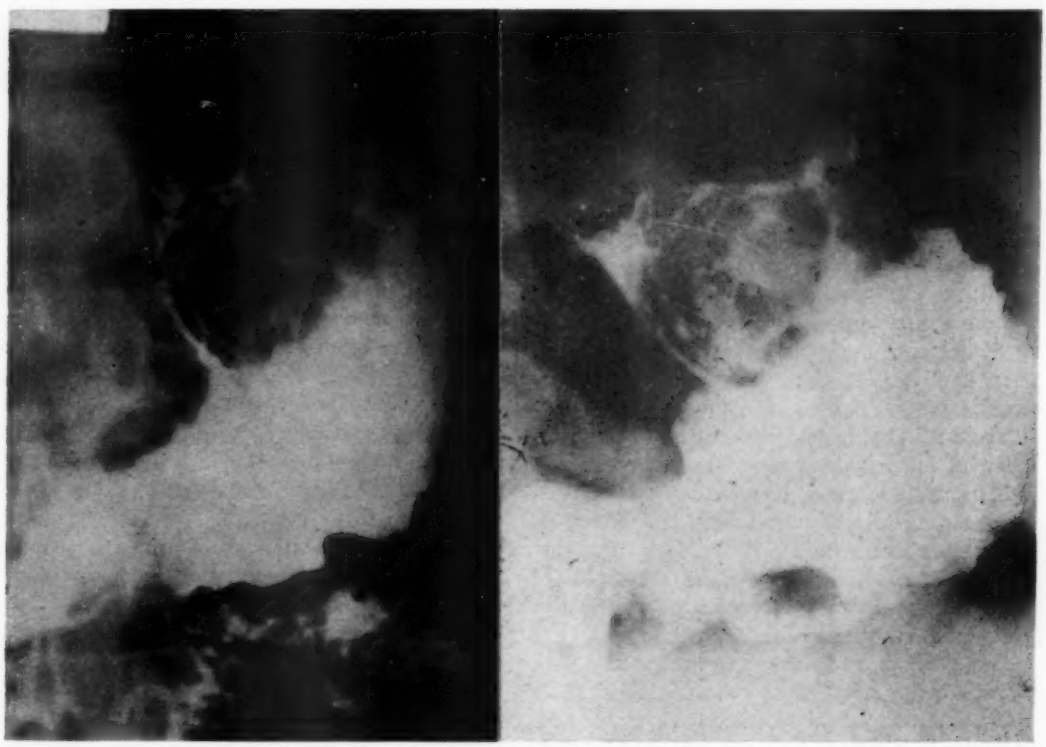

Fig. 2. Case 4.

On July 23, 1942 (left) there is demonstrated a large tumor mass in the cardia. On November 12, 1942, a "spot film" shows no change in the size of the mass. Its surface shows shallow lobulation. Note the large folds in the body of the stomach. The diagnosis was thought to be leiomyoma or lymphoma. The appearance is due largely to hypertrophic gastritis.

ing lesions like those of scirrhous carcinoma, lymphblastoma and syphilis." This is in agreement with the expressions of Martin, and Weber, Kirklin and Pugh in their articles on lymphoblastoma of the gastrointestinal tract.

Localized Thick Folds

When the thickening of the folds is localized, a correct diagnosis may be more difficult. Since most carcinomas of the stomach start in the antrum, the finding of thick folds in this region is an ominous roentgenologic sign, especially if the evidence persists over a period of several weeks.

The enlarged folds may end abruptly towards the body of the stomach but usually fade off gradually. They may take an oblique, almost transverse course, or may run parallel with the antral axis. Pearl and Brunn (14) have shown cases of gastritis with folds so large and segmented that the appearance of multiple nodular growths was created, simulating polyposis or cancer. When the folds are enlarged they are also fewer in number. The involved area is usually rigid so that the folds may be apparent even through the filled stomach. The lumen of the antrum may be narrowed and markedly distorted. Even moderate changes will produce irregularities in the contour of the antrum when the stomach is filled perhaps due to constant spastic contractions. Peristaltic waves pass through the diseased area poorly if at all. Gastric retention is a frequent finding.

Case 5

A white male aged 30 was admitted on March 16, 1945 complaining of pain in the epigastrium. This had been present intermittently for 9 months. He drank alcoholic liquors moderately. His past medical history was otherwise inconsequential. He began to have sharp pain in the right upper quadrant and epigastrium, and occasionally diffusely in the abdomen, in July 1944. The pain, which would come on daily from one to three hours after meals was usually associated with pyrosis, nausea, and occasionally vomiting. The ingestion of milk or ice cream would relieve the pain, but the usual meals would not. Tincture of belladonna afforded the greatest relief. This episode lasted for two months. From the end of September until December 1944 he was careful to avoid greasy or spicy foods, and was free of symptoms. In December, during his voyage to England, he had another episode of severe diffuse pain, coming on from one to two hours after meals. He was admitted to a hospital and thence sent to a General Hospital. The physical examination was negative except for tenderness over the mid-epigastrium and the right upper quadrant. Gastric analysis showed normal free and total acid. On April 2, 1945 there was 3 plus occult blood in his stool. The blood Kahn and Wasserman reactions were negative. The blood count and urine analysis were normal.

Roentgenologically the antrum of the stomach was irregular in contour. The folds were very prominent and stiff. Peristalsis passed through this region but moderate rigidity was apparent. Mucosal relief studies showed what appeared to be thick wavy segmented folds in at least the distal half of the stomach. The duodenal bulb was contracted, and its folds were large and distorted. There was no evidence of an ulcer in the stomach or duodenal bulb.

Gastroscopy showed the antral folds to be more prominent than usual. The gastric rugae were large and had a cobblestone appearance on the greater curvature and posterior wall of the middle and distal portions of the body of the stomach. Some of the folds were markedly elevated and segmented. There were no erosions or hemorrhages. The diagnosis was chronic hypertrophic gastritis, moderately severe.

Comment

Konjetzny (9) believes that the erosive form of hypertrophic gastritis is confined to the antrum. He also thinks that it is found in every case of gastric and duodenal ulcer, and has termed it, therefore, "ulcer gastritis." Schindler (16) on the other hand, has seen it more often in the body of the stomach and denies that it occurs in every case of peptic ulcer. He believes that only a localized gastritis is seen in the beginning. After a few months the pain increases, and a rather large ulcer is found gastroscopically in the area of hypertrophic gastritis. A short time later, the ulcer disappears. A true ulcer never develops, he states, hence, ulcerative gastritis and chronic gastric ulcer are different entities. Benedict and Mallory found that the gastroscopist made most of his errors when gastritis was confined to the antrum.

Case 6—*J.G. Age* 52 *MSH* 453859

This patient has intermittent gastrointestinal complaints unrelated to food. He had lost 14 lbs. in the past 3 months.

Roentgenologically there was persistent narrowing of the gastric antrum with preservation of large but otherwise normal folds. There was a

persistent fleck of barium near the proximal portion of the narrowed site probably due to an ulcer. Roentgenologically this was considered due to gastritis and ulcer.

A sub-total gastrectomy was performed. The examination of the speciman showed an ulcer measuring 1.3 by 2 by .5 cm., about 3 cm. from the pylorus about the middle of the lesser curvature. The mucosa distal to the ulcer gave evidence of severe hypertrophic gastritis with considerable hyperemia and petechial hemorrhages.

Comment

The prominent roentgenologic features in this case were the marked changes in the antrum. Pathologically, the prominent features were the size of, and the induration about, the ulcer. This case is similar to Case 6 in that the abnormal folds ended abruptly. Because of somewhat similar roentgenologic features but differing etiology the following case is presented.

Case 7–*S.E. MSH* 524315

This 50 year old white male was first admitted on August 28, 1944, with a history of belching, epigastric distress, and occasional nausea and vomiting for about 6 months. He had marked anorexia and had lost about 15 lbs. in weight. There had been no melena, hematemesis or fever. The patient was thin. Th physical examination revealed no other positive findings. His blood count, urine analysis, blood urea nitrogen, total protein, CO2 combining power, ECG, BMR and sedimentation rate were normal. His Wassermann reaction and stool guaiac test were negative. Free HC1 was obtained on gastric analysis after histamine.

Roentgenologically (Fig. 3) there was marked thickening of the antral folds which converged to a point on the posterior wall near the pylorus. The lesser curvature was shortened and the pylorus was eccentric in position. The findings were thought to be more consistent with a diagnosis of hypertrophic gastritis, although a neoplasm could not be excluded.

On gastroscopy the mucosa of the lesser curvature aspect of the prepyloric region was thickened and nodular, but normal in color. Peristalsis exaggerated the folds. The mucosa of the greater curvature of the antrum was normal. The rugae of the corpus were prominent, the mucosa was thickened and cobblestone in appearance. The gastroscopist suggested antral gastritis as a diagnosis, but could not exclude a neoplasm. The patient was discharged to be readmitted and restudied in 6 weeks.

He was readmitted on February 21, 1945 because of vomiting and tarry stools of 10 days duration. He had felt well until the onset of the present episode. He had lost 12 lbs. in wight. Except for the obvious loss of weight the physical examination was negative. The stool guaiac was 4 plus. All of his blood studies were again normal. Gastric analysis showed a high normal free acid and total acid. There was no blood in the gastric contents.

Gastroscopically, an ulcerated lesion with a yellow base and a thick everted edge was found

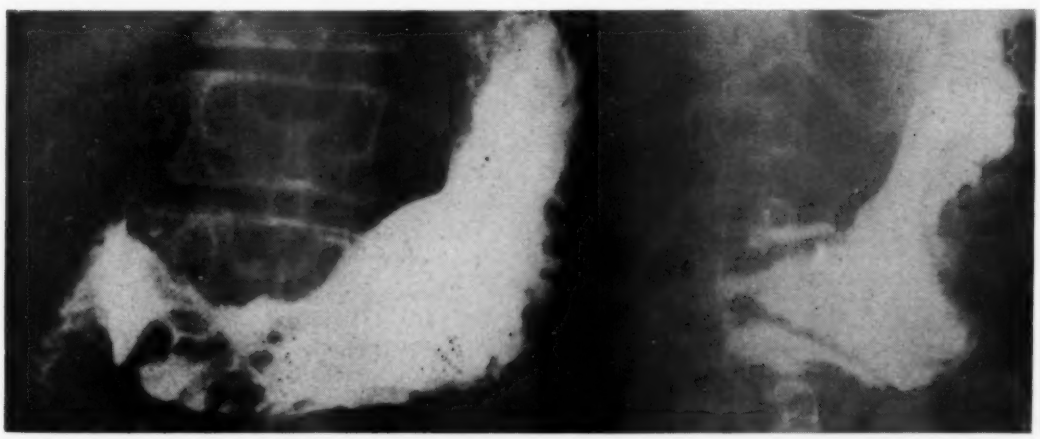

Fig. 3. *Case* 7.

(Left) The folds in the antrum are large and seem to radiate from a large ulcer crater. (right) Note the particularly large folds which are demonstrated. They are not continuous with the normal folds. This appearance was due to an ulcerating cancer.

on the greater curvature aspect of the pre-pyloric region. A thick ridge on the anterior wall extended to the lesser curvature. The diagnosis was cancer.

The patient signed out to be operated upon by his private physician and cancer was found.

The enlarged folds and the ulcer were the prominent roentgenological features in this case, much as in the previous case. The folds in this last case radiated for a considerable distance, going against the "grain" of the normal rugal pattern, and simulating the appearance seen in some benign ulcers. The roentgenologic appearance could not be differentiated from cancer.

Thick folds on the greater curvature

Normally the mucosal folds are more prominent on the greater curvature aspect of the body of the stomach, particularly when the stomach is not fully distended and is examined in the prone position. The greater curvature of the stomach is capable of greater distention than any other portion of the stomach. When the stomach is empty or incompletely filled, the gathering of the folds produces prominences in its contour. The sling-like muscle bundles which are seen on end in this region also contribute to the irregularity of the coutour.

These prominent folds, usually seen in a stomach with good tonus are always considered possibly abnormal by the fluoroscopist. It is only when the folds can be flattened by distention or smoothed out by manual manipulation, or by the weight of the barium suspension in the erect posture, that they may be disregarded.

When these folds become unduly prominent they may easily be mistaken for a neoplasm. Too many such cases have been operated upon under the mistaken diagnosis of cancer. When the folds are large they are stiffer than normal, and persistent in all studies, whether of the mucosa or of the moderately distended stomach. Occasionally one sees carcinoma simulating this picture, and the differentiation is extremely dfficult.

Case 8 *D.D.*

This elderly individual gave a history of diarrhea with blood in his stools for the past 5 years. He had lost 10 lbs. in weight. None of his other complaints were referable to his gastrointestinal tract. Roentgenologic examination by his physician disclosed a serrated greater curvature of the body of the stomach with thick folds which seemed to end abruptly at the midportion of the stomach.

Fig. 4. Case 7.

The serration of the greater curvature aspect of the body and fundus was believed to be due to cancer. At operation, only large folds were found. There was no evidence of neoplasm.

Fig. 4. A diagnosis of cancer was made. At operation, only large folds were found.

Thick folds which eventually disappear.

Case 9. A 27 year old white male was admitted on July 5 complaining of being tired and weak, and having pain in the stomach and gaseous feeling for 3 or 4 weeks. He had been in the Army for 28 months. He drank several glasses of beer a week, and smoked a half pack of cigarettes a day.

He had been given yellow fever vaccine on July 14, 1942, and developed hepatitis in September of that year. A roentgenologic examination of his stomach in February, 1943, was reported as normal (Fig. 5a). The reasons for requesting this examination do not appear on his chart. He was discharged to duty on March 31, 1943.

Soon after discharge he began to have a dull aching pain in his epigastrium and right upper

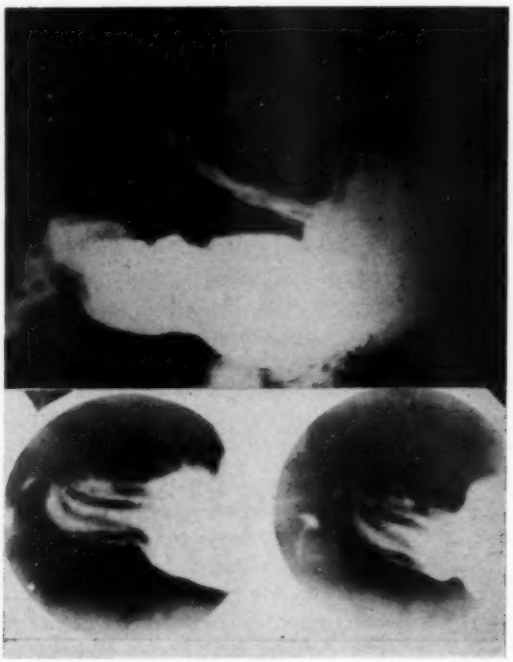

Fig. 5A.

Fig. 5. Case 9.
(a) On February 16, 1943 the gastric antrum was normal.
(b) To right; on July 14, 1943 the antrum was persistently conically narrowed and moderately rigid. Peristalsis did not pass through this area. On compression the antral folds were seen to be thick, sinuous and decreased in number. To left; after medical treatment, the antrum and its folds were seen to be normal on July 26, 1943.

quadrant. The pain usually, but not invariably, came on after meals. He had frequent attacks of nausea and vomiting. These symptoms were worse after fatty meals. His appetite was poor for the two weeks prior to his readmission. He had lost 4 lbs. in the three months following his discharge from the hospital. He did not notice anything unusual about his stools.

No unusual findings were elicited on physical examination. His liver and spleen were not palpable. On two occasions after his readmission the gastric analysis showed no free acid, and the highest total acid was 26. There was no occult blood in the feces. His blood count was 4,850,000 red corpuscles per cu. mm. with 95 per cent hemoglobin, 9,500 white cells and a differential count of 61 per cent polymorphonuclear leuko-

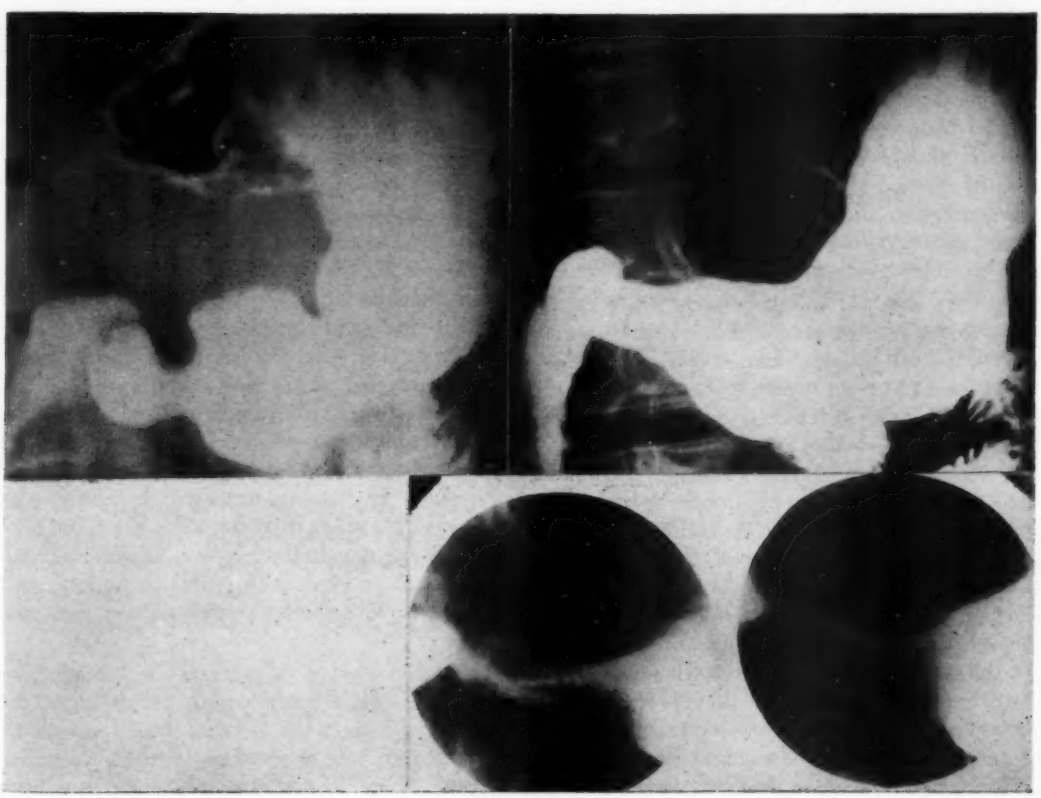

Fig. 5B.

cytes and 35 per cent lymphocytes. His icteric index was 7, and his blood Wassermann reaction was negative.

Roentgenologic examination of the stomach and duodenum (Fig. 5b) showed the gastric antrum to be persistently narrowed, somewhat rigid and smooth in outline, through which peristalsis did not pass. The antrum could not be distended to its normal caliber. The antral folds were decreased in number, thick wavy in outline, and somewhat rigid. In view of the history, particularly the absence of free HCl in the gastric secretions, an infiltrating submucosal lesion was suggested, possibly neoplasm.

Gastroscopy performed in July showed a diffuse gastritis-like lesion in the antrum, hypertrophic in type. The gastroscopist could not exclude a neoplasm, however. The patient was treated symptomatically for 12 days and then re-examined. At this time the antrum was normal in all respects (Fig. 5b). The mucosal folds were normal. The patient was discharged with a diagnosis of acute antral gastritis.

Comment

Gutmann, Beaugart and Hardel (6) reported a case with a similar roentgenologic appearance in a 28 year old male who had been drinking heavily. The antral folds were markedly thickened, hazy in outline and rigid. A diagnosis of infiltrating neoplasm was seriously considered but was discharged when, after two weeks of medical treatment, the folds and the antrum were found to be normal. Their final diagnosis was "acute edematous gastritis.'

In these cases of enlarged somewhat rigid antral folds, not associated with ulcer, one cannot, on the basis of a single examination, differentiate between cancer and gastritis, except that the mucosal folds in infiltrating submucosal cancer are often of normal caliber. Slow progression of the roentgenologic changes, despite treatment, does not serve to differentiate cancer from a benign lesion, as shown by case 2. Only definite regression in a short interval would justify a diagnosis of gastritis as against cancer. Pathologically there is an infiltration of the superficial aspects of the mucosa, mainly about the necks of the glands. Superficial hemorrhages and surface erosions may be present. Varying amounts of mucus may cover the inflamed surface. In severe cases the deeper layers may be involved. It is an acute exudative process which may be superimposed on other forms (1).

Of 9 patients with infectious hepatitits, Knight and Cogswell (8) found 7 with abnormal gastroscopic findings. These consisted of aphthous ulcerations and other aspects of superficial gastritis. The antrum was involved in all. The abnormal changes often extend into the fundus. Peristalsis was not interfered with.

Little is known about the roentgenologic appearance in superficial gastritis since the changes are most often too insignificant to produce roengenologic changes (17). Templeton quotes Berg as stating that considerable mucus, occasional rugal enlargement and hypermotility may be present. If there are abnormal folds which do not end abruptly, and which return to normal in two to four weeks, a diagnosis of gastritis can be made.

Summary

The range of variations in the caliber of the normal gastric rugae is considerable, and therefore open to roentgenologic misinterpretation.

It is most important to determine whether or not a cancer is present. It has been said that in gastritis the folds have sharp borders and that their course remains unchanged even when the changes are most marked. The abnormal folds course in the same direction as do the normal folds. There is no abrupt change as in carcinoma. We have seen exceptions to this rule, however.

The prominence of the mucosal folds depends chiefly on changes occurring in the submucosa. Hence any disease which will increase the volume of the submucosa will effect the appearance of the mucosal pattern. More importance should be attached to the loss of pliability (rigidity) than to change in size alone.

Generalized enlargement of the gastric rugae is probably most often due to gastritis. Swelling and distortion of the duodenal folds is usually also present. In some cases presenting this appearance the gastroscopic appearance of the mucosa may be normal, but there is evidence to suggest that there may be cases of interstitial gastritis in which the mucosa is not involved. Lymphoblastoma may also produce a generalized enlargement of the gastric rugae and duodenal folds.

When the rugal enlargement is localized, or when there is a complicating gastric ulcer, the differential diagnosis is hazardous. Laparotomy may be indicated to avoid neglecting a resectable cancer. Some of the cases of benign rugal enlargement which are localized are so like cancer

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that any other diagnosis is hardly considered. The differential diagnosis must also include lymphoma and syphilis.

In the group of cases here reported, the patients complained of symptoms which could not be explained except on the basis of "chronic gastritis."

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A COMPARISON OF PERITRATE[R] AND OTHER ORGANIC NITRATES IN THE TREATMENT OF ANGINA PECTORIS*

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When the ealy clinical experience with Peritrate[R] (1.2) in this country confirmed the impression of the French workers (3-5) that this drug was effective in controlling angina pectoris, a study was undertaken to compare the therapeutic and toxic effects of Peritrate[R] with other previously used organic nitrates.

Peritrate[R] is an explosive belonging to the same group as nitroglycerin, mannitol hexanitrate and erythritol tetranitrate. Its safety in animals and man has been thoroughly established by the United States Public Health Service. (6)

Methods and Results

Twenty-nine private patients with well-documented coronary arteriosclerotic heart disease with anginal syndrone who had previously taken erythritol tetranitrate and/or mannitol hexanitrate were given Peritrate[R] in doses of 10 mg. before each meal and 10 mg. at bedtime. One patient was started on 10 mg. T.I.D. The dose was increased to 20 mg. before each meal and 20 mg. at bedtime in 8 patients. The average duration of treatment was 10 months, the range being from 7 to 14 months.

Comparisons were made as to the effectiveness of the 3 drugs (Peritrate[R], erythritol tetranitrate and mannitol hexanitrate) on the control of symptoms and on the incidence and type of toxic effects (Table I). Only 2 of the 29 patients experienced any type of toxic effect from the Peritrate[R] (Cases 22 and 23). Case 22 was a 75 year old female who had 2 myocardial infarctions and severe anginal syndrome. It is pertinent to note that this patient could not tolerate erythritol tetranitrate because of headache. This patient could tolerate no more than gr. 1/400 of nitroglycerin. Nitroglycerin gr. 1/200 produced headache. The nausea and headache which she experienced was severe enough to stop the drug (Table I). Case 23 was a 61 year old female who had severe diabetes mellitus and coronary arteriosclerotic heart disease with anginal syndrome. This lady could not tolerate erythritol tetranitrate but she was able to take mannitol hexanitrate 100 mg. Q.I.D. Peritrate[R] produced slight nausea which did not warrant cessation of medication (Table I). However, the Peritrate[R] was discontinued in this patient because the lack of therapeutic effectiveness did not warrant further treatment.

Ten patients tolerated both Peritrate[R] and erythritol tetranitrate (Table II). Five patients were equally improved with both (Cases 4, 11, 16, 21, and 26). Two (Cases 17 and 19) of these 10 patients were better improved with Peritrate[R] and 3 (Cases 8, 10 and 18) were not helped by either.

Fourteen patients tolerated the Peritrate[R] but not erythritol tetranitrate (Table II). Four of these patients were aqually improved by both (Cases 1, 3, 24 and 28). Nine of these 14 patients were better improved by erythritol tetranitrate (Cases 2, 5, 6, 13, 15, 20, 25, 27 and 29). One of these patients was not helped by either drug

*Peritrate (R), designated as CH-27 during clinical investigation, was supplied by Chilcott Laboratories, Morris Plains, New Jersey.

TABLE I

CASE NO.	AGE	SEX	Erythritol Tetranitrate			Nitroglycerin			Mannitol Hexanitrate			Peritrate(R)		
			Dose Gr.	Side Effect	Effects	Dose Gr.	Side Effect	Effects	Dose Mg.	Side Effect	Effects	Dose Mg.	Side Effect	Effects
1	59	F	¼ QID	Occasional Headache		1-200 1-150	None Headache	Good Good				10 QID 20 QID	None None	
2	47	M	¼ QID ⅛ QID	Headache None	Good Good	1-200 1-400	Headache None	Good Good				10 QID	None	Excellent
3	39	M	⅛ QID ¼ QID	No Headache Headache	Good	1-200 1-400	Headache No Headache	Good Good				10 QID 20 QID	None None	Good Good
4	62	F	¼ QID ½ QID	None None	Good Good							10 QID	None	Good
5	71	M	¼ QID	Headache	Poor	1-150 1-200	Headache None	Good Good				10 QID	None	Good
6	58	M	¼ BID ½ TID	Headache Headache	Poor Poor	1-150	Headache	Good				10 QID	None	Excellent
7	71	F				1-200 1-400	Headache Headache	Good Good	100 TID	Headache	Poor	10 QID	None	Excellent
8	42	M	¼ QID	None	Poor	1-150	None	Good				10 QID 20 QID	None None	Poor Fair
9	52	M	¼ QID ⅛ QID	Headache None	Poor Poor	1-200	None	Good				10 QID 20 QID	None None	Poor Fair
10	62	M	½ QID	None	Poor	1-150	None	Good				10 QID 20 QID	None None	Poor Fair
11	46	F	½ QID	None	Good	1-150	None	Good				10 QID	None	Good
12	56	M				1-150	Headache	Good	100 TID	Headache	Poor	10 QID	None	Good
13	58	M	⅓ TID	Headache	Poor	1-100 1-200	Headache None	Good Good				10 QID	None	Good
14	62	M	¼ QID	Headache	Poor	1-100 1-200	Headache None	Good Good	100 TID	Headache	Poor	10 QID	None	Good
15	49	M	⅛ QID ¼ QID	None Headache	Poor Poor	1-200 1-400	Oc. H'dache None	Good Fair				10 QID	None	Good
16	54	M	¼ QID	None	Good	1-150	None	Good				10 QID	None	Good
17	59	F	¼ QID	None	Fair	1-200	None	Good				10 TID	None	Good
18	41	M	½ TID	None	Poor	1-150	None	Good				10 QID	None	Poor
19	42	M	⅓ TID	None	Poor	1-150 1-200	Oc. H'dache None	Good Good				10 QID	None	Good
20	43	M	⅛ QID ⅓ TID	None Headache		1-200	None	Good				10 QID 20 QID	None None	Good Good
21	49	M	⅓ TID	None		1-150	None	Good				10 QID	None	
22	75	F	¼ QID	Headache		1-200 1-400	Headache None	Good Good				10 QID	Nausea & Headache	Poor
23	61	F	¼ QID	Occasional Headache	Fair	1-200	None	Good	100 QID	None	Fair	10 QID	Slight Nausea	Fair
24	64	M	¼ QID ½ QID	None Headache	Good Good	1-200	None	Good				10 QID	None	Good
25	62	M	⅛ QID	Severe Headache	Poor	1-200	None	Good				10 QID 20 QID	None None	Good Excellent
26	64	M	⅛ QID	None	Good	1-200	None	Good				10 QID	None	Good
27	46	M	⅛ QID Higher Doses	None Headache	Poor Poor	1-150 1-200	None None	Good Good				10 QID	None	Good
*28	55	F	⅛ TID ¼ QID	None Headache	Good Good	1-200	None	Good				10 QID	None	Good
**29	50	M	¼ QID ⅛QID	None Headache	Poor Poor	1-200	None	Good				10 QID 20 QID	None None	Fair Good

*Patient died of acute myocardial infarction after 8 months on Peritrate(R).
**Patient died of acute myocardial infarction after 7 months on Peritrate(R).

TABLE II

	Total Number of Patients	Equally Improved With Both	Better Improved With Peritrate	Neither Helped
Tolerated both Peritrate® & Erythritol Tetranitrate	10	5	2	3
Tolerated Peritrate® but not Erythritol Tetranitrate	14	4	9	1
Tolerated Peritrate® but not Mannitol Hexanitrate	2		2	
Tolerated Peritrate® but not Mannitol Hexanitrate or Erythritol Tetranitrate	1		1	
TOTALS	27	9	14	4

(Case 9). Two patients tolerated Peritrate® but not mannitol hexanitrate. Both of these patients were better improved with the Peritrate® (Cases 7 and 12). One patient tolerated Peritrate but not mannitol hexanitrate or erythritol tetranitrate (Case 14), and this patient noted better improvement with the Peritrate®.

The difficulty in evaluating therapy in angina pectoris is well known. No attempt was made to use placebos or controls in any way. The primary purpose of the study was to compare the toxicity and the effectiveness of Peritrate® as contrasted with erythritol tetranitrate. Criteria for effectiveness of the Peritrate® and the other organic nitrates (erythritol tetranitrate and mannitol hexanitrate) used in this study were: (1) decrease in number of anginal attacks and (2) decrease in nitroglycerin requirement. Protection from attacks of angina pectoris decubitus was considered an "excellent" effect. Patients classified as having "good" results from the organic nitrates were those in whom the nitroglycerin requirement was definitely decreased. The results were considered "fair' when the nitroglycerin requirement was less markedly decreased and when such medication offered the patient sufficient improvement to worth the expense and trouble of taking the tablets. "Poor" results were those in which the organic nitrates were without therapeutic effect. In a few patients the effect of the organic nitrates could not be evaluated (Table I).

Toxic effects, however, are easy to determine. The striking result of this study was that only 2 of the 29 patients experienced unpleasant effects from the Peritrate®, and both of these patients had previously been unable to tolerate erythritol tetranitrate. On the other hand, 17 of these 29 patients could not tolerate either erythritol tetranitrate or mannitol hexanitrate because of headache. Table II shows that Peritrate® probably is more effective therapeutically than erythritol tetranitrate and much less toxic.

The clinical experience described herein and reports of Winsor and Humphreys, (7) Perlman,(8) Samuels and Padernacht(9) and Plotz (10) indicate that Peritrate is an effective coronary vasodilator worthwhile in the treatment of angina pectoris and in the other painful syndromes of coronary arteriosclerotic heart disease. These studies confirm the animal experiments that Peritrate® is less toxic than erythritol tearanitrate.(6).

Summary and Conclusions

Peritrate® was administered to 29 patients with well-documented angina pectoris who had received erythritol tetranitrate and/or mannitol hexanitrate previously. Nineteen of these patients had experienced headache after taking erythritol tetranitrate or mannitol hexanitrate, but only 2 patients experienced unpleasant symptoms with Peritrate®. Both of these patients had been unable to tolerate erythritol tetranitrate previously. One was a 75 year old female who experienced nausea and headache on Peritrate®. The other was 61 year old female who noted some slight nausea after taking Peritrate®. Peritrate® appears to be less toxic and more effective than erythritol tetranitrate in the treatment of angina pectoris.

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BASIC *Science* SEMINAR

PHYSIOLOGY OF THE PANCREAS (EXOCRINE)

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I ANATOMY
II HISTOLOGY
III PHYSIOLOGY

A) *Classic theories of exocrine pancreatic Physiology*
1) Volume of pancreatic juice
2) Composition of pancreatic juice
3) Ferments of pancreatic juice
   a) Pancreatic proteinases
   b) Pancreatic amylase
   c) Pancreatic lipase
   d) Pancreatic rennin
4) The regulation of the secretion of pancreatic juice
   a) Hormonal control
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B) *Recent work on the physiology of the pancreas*

PHYSIOLOGY OF THE PANCREAS

It would seem necessary to give a description of the anatomy and of the histology of the pancreas for a better understanding of the physiology of this organ. *Anatomy*: The pancreas is an elongated, hammer-shaped gland; it lies in the epigastrium and left hypochondrium in an ultimately retroperitoneal position behind the serosal floor of the omental bursa, at the level of the first and second lumbar vertebrae. The pancreas is divided into a head, neck, body and tail. Two ducts collect the secretions of the pancreas; the main pancreatic duct of Wirsung and the accessory pancreatic duct of Santorini. The body and tail of the pancreas derive most of their rich arterial circulation from the splenic artery. The head is supplied largely by the anastamosing superior and inferior pancreaticoduodenal trunks from the gastroduodenal and superior pancreatico duodenal arteries respectively. The veins of the pancreas join the splenic vein, but a large trunk issues from the dorsal aspect of the gland and runs upward along the left of the common bile duct to join the portal vein. This vessel may be injured in exposure of the pancreatic part of the common duct. Scarcely an organ in the abdomen possesses as extensive a lymphatic distribution as does the pancreas. Its nerves are filaments from the lineal plexus or splenic plexus which is formed by branches from the celiac plexus, the left celiac ganglion and from the right vagus nerve. (1) (2).

Histology: Structurally as well as physiologically the pancreas may be divided into two portions: (1) the acinar system having to do with the secretion of digestive juices poured into the duodenum through the ducts of Wirsung and Santorini, (2) the islands of Langerhans or the interacinar system having to do with the secretion of insulin, which is the internal secretion concerned with sugar metabolism. The purpose of this paper is to study physiologically the pancreas as an exocrine gland only. The pancreas is a racemose gland, its alveoli resembling those of the salivary gland in their general arrangement and design. Lying between the alveoli are groups of cells constituting the islands of Langerhans. The cells which line the alveoli and furnish the ferments of the pancreatic juice, contain, like the serous cells of the salivary glands and the chief cells of gastric tubules, zymogen granules. During fasting the granules accumulate until eventually they almost completely fill the cell, but dur-

ing digestion they disappear with the discharge of the secretion, the width of the granular zone gradually decreasing. The secretion collected by a system of ducts leading to the duct of Wirsung and Santorini discharges in company with the common bile duct into the ampulla of Vater, and for the duct of Santorini, ¾ inch above the duct of Wirsung. (3) (4).

PHYSIOLOGY

(1) *Volume of Pancreatic Juice.*

A twenty-four hour output of approximately a liter or more of pancreatic juice has been reported in patients with fistulous tract by Monat (6), Kahn and Klein (7) and Snyder and Lium (8). In one day Snyder and Lium's case secreted as much as 1400 cc. of pancreatic juice. Despite the reports of smaller amounts, it seems safe to say that the average daily secretion is well in excess of one liter and that is it difficult to say how much, exactly, pancreatic juice is secreted in 24 hours by the normal human subject. (5) But the physiologist is able now to give a very good approximation by measuring directly the flow of pancreatic juice by canulating the pancreating duct. The volume of secretion for a period of sixty minutes after the administration of 80 units of secretin is the following:

	In Normal Patients	In Patients With Relapsing Pancreatitis	In Patients Having Chronically Diseased Pancreas
	CC.	CC.	CC.
Maximum	301	337	322
Mean	152	137	102
Minimum	75	34	4

Since the rate of pancreatic flow in the pathologic group is practically identical to the rate of flow in the normal group, it is tempting to suggest that the total volume of secretion may be a measure of the mass of functioning pancreatic cells. (9) Moderate increases in temperature favor an increased flow of pancreatic juice, whereas marked elevations cause a decrease. A low carbohydrate diet combined with large amounts of sodium bicarbonate so reduces the amount of pancreatic secretion as to be a valuable therapeutic measure in the closing of the fistulae. Secretions low in enzymes may be obtained by the oral administration of hydrochloric acid or water. Sodium bicarbonate seems to decrease pancreatic secretion and so do atropine, ephedrine and epinephrine. Pilocarpine and physostigmine produce increased secretion with a more viscous juice evidencing a greater proteolytic power.

The composition of pancreatic juice

The composition of pancreatic juice is given in the following tables. Its pH is between 7.10 and 8.20 (in dog). In human T. H. McGavack gives a pH lying between 8.0 and 9.0, changing within slight limits, in relation to the type of foodstuffs undergoing digestion.

(Modified from Starling)

	Secretin juice from three dogs (Sp. gr. 1014)	Pilocarpine Juice
Alkalinity; number of cc. of NaOH N/10 equal to 10 cc. juice	12.7	5.5
Total solids in 100 cc.	1.58 gm.	6.4
Total proteins in 100 cc.	0.5	4.8
Ash in 100 cc.	0.96	1.3
Chlorides in 100 cc.	0.30	0.27
Total nitrogen	——	0.74

The ferments of pancreatic juice are trypsin, chymotryspin, amylase, lipase, rennin, and maltase.

Pancreatic proteinases

There are at least two proteinases in pancreatic juice; trypsin and chymotrypsin. Trypsin is not secreted as such but in an inactive form called trypsinogen. The activation was first shown by Schepowalnikow in Pavlov's laboratory to be brought about by the addition to pancreatic juice of a small quantity of intestinal juice or an extract of the intestinal mucosa. The activation is due to an enzyme called enterokinase. Trypsinogen undergoes spontaneous transformation to trypsin when the pancreas is allowed to stand in a slightly acid solution. Pure trypsinogen is also activated by the addition of trypsin, or of magnesium or ammonium sulfate.

The spontaneous activation of trypsin is greatly accelerated by the presence of a calcium salt.

Chymotrypsin is also secreted in an inactive form: chymotrypsinogen, and is activated by trypsin but not by enterokinase.

These two enzymes, trypsin and chymotrypsin, are mainly responsible for the proteolytic activity of pancreatic juice. Both enzymes are proteins and they have been obtained in pure crystalline form. The optimum pH for the action of trypsin and of chymotrypsin is around 8; that of enterokinase is within the range between pH 5.2 to pH 6.0. The action of trypsin carries the digestion of protein beyond the stage of pepton. It also differs from peptic digestion in being carried on in an alkaline instead of in an acid medium. Though under ordnary circumstances trypsin is called upon to commence its action after the gastric juice has converted a large part of the protein into proteose and peptones, it can also at-

tack native protein; flesh introduced directly into the duodenum is readily digested by the pancreatic juice. Nevertheless, the preparatory digestion of protein by gastric juice is favorable to tryptic action. The specific action of trypsin is to break the proteose and peptone fragments of the protein molecule into smaller amino-acid groups. These are generally termed 'peptids." In the earlier stages of tryptic digestion the amino acid groups are for the most part still relatively large polypeptides. Some of these are later split into groups containing 2, 3 or 4 amino acids, constituting the dipeptids, tripeptids and tetrapeptids; even a few individual amino-acids such as tyrosine and tryptophane are released. The complete breakdown of protein is reserved for the erepsin of the succus entericus. The pancreatic juice also contains a small amount of an enzyme similar in action to erepsin. (4) Le Breton and Mocoroa demonstrated that normal pancreatic juice contains the following proteiolytic ferments: (a) a tryptase in the state of an inactive proferment; activated by the kinase, this enzyme breaks the proteins into amino-acids and some polypeptids. (b) a protaminase directly active which hydrolyses the protamine to liberate arginine. (c) a carboxypolypeptidase directly active which breaks polypeptides. Of those 3 ferments the typtase plays the most important role. ((11).

Pancreatic amylase

This has an action similar to but much more powerful that that of salivary amylase (ptyalin). In the hydrolysis of starch by pancreatic juice the same stages are passed through as for salivary digestion, but they are completed in a fraction of the time, most of the starch being converted into maltose within a few minutes. Due to traces of maltase small amounts of glucose are also formed in the final stages of the pancreatic digestion of starch. Pancreatic amylase unlike the corresponding salivary enzyme is capable of digesting unboiled starch. Raw corn and wheat may be converted entirely into maltose, and raw potato starch is transformed to the extent of 80 per cent. It is important to remember in connecion with infant feeding that during the first few weeks of life pancreatic amylase, the only really efficient ferment for the digestion of starches, is absent from the pancreatic juice. Little provision has been made for the digestion at this time of any other food than the natural one: milk.

The amylotic ferment of the pancreas acts in a neutral slightly alkaline or slightly acid medium. It acts to best advantage when the medium is faintly acid or neutral in reaction, its pH optimum ranging from 6.7 to 7.0. Certain inorganic ions, especially Cl, are absolutely essential for its action; if these be separated from pancreatic juice by dialysis, the juice is deprived of its starch splitting power. Part of the amylase is believed to be reabsorbed from the intestine and excreted in the urine.

Pancreatic lipase

This is a fat splitting enzyme. It has the power

PANCREATIC SECRETION IN MAN AFTER STIMULATION WITH SECRETIN AND ACETYL-BETA-METHYLCHOLINE CHLORIDE (10)

Substance	Total Duodenal Contents in cc. 70 Min. period	Peak Period in Min.	Amount in Peak Period In cc.	pH	Amlase Total 70 min.	Amlase In Gm. per cc. at P.P.	Amlase Maltose Total P.P.	Peak at Min.
Fasting	8.78 (10 Min.)			7.05		1.3		
Secretin (humoral Stim.)	151.3	1-20	32.33	8.00	104.05	0.318	8.83	10-20
Mecholyl chloride (vagal stim.)	58.4	1-30	40.8	7.05 (approx.)	210.68	3.790	181.01	0-40

Substance	Secretion of Trypsin in CC. N/10 KOH				Secretion of Lipase in CC. N/220 NaOH			
	Total 70 Min.	Per cc. at P.P.	Total P.P.	Peak at Min.	Total 70 Min.	Per cc. at P.P.	Total P.P.	Peak at Min.
Fasting		1.60				76		
Secretin	148.0	0.60	16.5	10-20	13,373	62	1,691	10-20
Mecholyl chloride	138.5	2.65	103.7	0-30	6,474	103	6,474	0-70

of splitting the neutral fats of the food by hydrolysis, into fatty acid and glycerol. A typical reaction would be as follows:

$$C_3H_5(00CC_{15}H_{31}) + 3H_2O \rightarrow 3\,(C_{15}H_{31}C00H) + C_3H_5(OH)_3$$

Palmitin — Palmitic acid — Glycerol

Pancreatic lipase is very unstable and is easily rendered inert by the action of acid. For this reason it is not possible to prepare an extract having a satisfactory fat splitting power from a pancreas which has been removed from the organism for a sufficiently long time to become acid in reaction.

Pancreatic lipase is undoubtedly the most important fat splitting enzyme in the digestive tract. In the absence of pancreatic lipase, as when the pancreatic duct is obstructed by disease, the fat of the diet appears in the undigested form in the feces; this condition is known as steatorrhea. The enzyme is water soluble and presumably a protein, although sufficiently pure preparations to prove this have not as yet been obtained, nor has the enzyme been crystallized. The action of the enzyme on fats is obviously dependent in large extent upon the surface of fat available; thus, the more highly emulsified the fat is, the more surface is exposed to the aqueous phase containing the enzyme and the more rapid is lipase action. Emulsification of fats in the digestive tract is facilitated by the presence of bile, because of the lowering of surface tension brought about by the bile salts. The bile also aids in fat digestion by aiding in the removal of the end products of lipase action. It is believed by some that the bile actually activates pancreatic lipase; it appears more probable that the acceleration in lipase activity in the presence of bile is due to physiochemical action of the bile salts in facilitating closer contact between the water-soluble lipase and the fat globule. (12).

Pancreatic rennin

Pancreatic rennin has an action similar to that of gastric rennin, but the pancreatic juice has a much more powerful milk-curdling power than has gastric juice. It is probable that this action is not due to a separate enzyme but to chymotrypsin.

The regulation of the secretion of pancreatic juice

The regulation of pancreatic juice is under both hormonal and nervous control.

—a) *Hormonal control*

Bayliss and Startling showed that an acid extract (HCL) of the duodenal mucosa when injected into the blood stream of an animal caused a copious flow of pancreatic juice. I. V. injection of the acid itself was ineffective. A secretoguogue effect also followed the introduction of acid into a loop of bowel whose nervous connections have been completely severed, the only communication between the bowel and the pancreas being then through the blood stream. The secretory effect was shown to be specific and not simply due to vasodilatation of the pancreatic vessels. *The excitatory substance was called secretin.* The obvious physiological implication of these results was that the acid chyme upon coming into contact with the duodenal mucosa caused the production, or liberation, of a substance which was then conveyed by the blood to the pancreatic cells.

Ivy, Farrell and Lueth transplanted a loop of intestine and the tail of the pancreas to subcutaneous sites, thus isolating the two structures completely from extrinsic nervous control. They obtained secretion from the pancreatic transplant when acid was placed in the isolated loop. Since the intra-venous injection of acid alone is ineffective, this experiment affords conclusive evidence for the liberation of a hormone from the intestinal mucosa.

Mellanby and Huggett demonstrated that secretin existed preformed in the mucosa from which it could be extracted by water, alcohol and other solvents as well as by acid. Bayliss and Starling had claimed that the hormone existed in an inactive or precursory form which they called prosecretin. Mellanby also found that bile introduced into the duodenum caused secretin to be absorbed into the blood stream and that the active agent in the bile was the cholic acid of the bile salts. He suggested that the bile salts in their passage through the intestinal mucosa absorbed the secretin and carried it into the blood. Bile salts, however, though aiding in the absorption of the hormone are not absolutely essential. Ivy and his colleagues have shown that food (meat and fat) entering the intestine stimulates pancreatic secretion in the usual manner after ligation of the common bile duct.

The action of secretin is not reduced by atropine which paralyzes vagal endings or by ergotamine which paralyzes sympathetic secretory fibers; so there is no evidence that its production or absorption is influenced by nervous mecha-

nisms, or that it stimulates parasympathetic terminals in the pancreas. It appears to be a direct excitant of the glandular cells. Secretin also stimulates the secretion of bile and probably of the succus entericus. Its cholalogue effect is a direct one and not simply secondary to the liberation of metabolites from the activated pancreas.

Ivy and Greengard have obtained secretin in the form of a crystalline picrolonate. The highest yield of secretin is given by the upper two-thirds of the small intestine. Minimal amounts are obtained from the lower third of the small intestine and from the ascending colon. It is absent from the gastric mucosa.

Harper and Raper have given the name of pancreozymin to a second pancreatic hormone obtained, like secretin, from duodenal mucosa. The existence of this hormone has been confirmed by Greengard and his associates. Unlike secretin, it stimulates the secretion of trypsin, amylase and lipase but exerts little or no effect upon the volume of secretion. It causes the discharge of the zymogen granules; its action is thus similar to that of the vagus though its effect is apparently a direct one upon the gland cells and not exerted through the nerve terminals for it is not altered by atropine. (4).

(b) *Nerve control*

It has been known since the important work of Pavlov on pancreatic secretion that the gland cells are excited by vagal impulses. This control of pancreatic secretion by the vagus was shown in the following way. The nerve was divided in the neck four days previously. This preliminary procedure has the effect of practically abolishing irritability of the cardiac fibers. When the nerve prepared in this way is stimulated, a well-marked secretion of juice occurs. The vagal secretion is rich in ferments. Indeed, the secretion of ferments is mainly under vagal control. The chief effect of secretin, on the other hand is to cause the secretion of the water and inorganic constituents, e.g., the bicarbonate of the pancreatic juice. Vagal stimulation causes exhaustion of the zymogen granules. Then, apparently, the extrusion of the colloidal zymogenous particles from the cells into the alveoli is largely controlled by nervous impulses. The hormone, on the other hand, causes a flow of alkaline fluid which serves to flush the alveoli, to thin the juice rich in organic material and sweep it along the ducts. Pilocarpine acts similarly to vagal stimulation. Atropine annuls the nervous secretion, but not that caused by secretin and pancreozymin. Stimulation of the splanchnic nerves was found by Harper and Vass to reduce the rate of secretion of pancreatic juice and the output of enzymes, but this may be secondary to a constrictor effect upon the vessels of the gland. They conclude that the sympathetic is either without effect upon pancreatic secretion or is inhibitory. (4)

Recent Works on the Physiology of the Pancreas

We have seen the classic theories of exocrine pancreatic physiology. Let us point out now some of the new experiments which modify or add to the classic picture. It was known before that secretin was liberated from the upper intestine by acids, but an acid was thought to be the most powerful and also the most important stimulus for the intestinal phase of pancreatic secretion. So far the experimental evidence does not exclude acid as an important stimulus for pancreatic secretion. However, some other foods produce a less acid intestinal content, notably fats; they do nevertheless, adequately stimulate the pancreas. Furthermore, some clinical investigators, McClure, C. W. and Christiansen, T., have pointed out that pancreatic secretion appears to be adequate in achlorhydria at least with respect to enzymes. Dr. Pincus and his co-workers at the Jefferson Medical College undertook a direct approach to the problem. They measured the volume of pancreatic juice secreted by dogs during measured time intervals while animals were digesting various types of meals and determined the pH of samples of intestinal contents collected during the same time intervals. They found, as have others, that both the volume of pancreatic juice and the intestinal pH varied from moment to moment to a considerable range. They confidently expected to find that these fluctations would be related to each other in such a way that an increase in volume in pancreatic juice would be associated with an intestinal acidity and vice versa. This did, in fact, happen on occasion, but just as often the volume increased while the acidity decreased, or the two showed no recognizable relationship whatever. This is sufficient to raise a reasonable doubt as to the validity of the classical viewpoint, particularly since it is based on an hypothesis only and not on experimental evidence.

Dr. Babkin advanced the hypothesis that an increase or decrease in the concentration of one enzyme is accompanied by a corresponding change in the concentration of all other enzymes.

In 1943, Grossman and Ivy reported a study on rats which seemed to show the relative concentrations of various enzymes in pancreatic tissue was not constant but varied with the diet. Dr. Beamer has tried similar experiments using dogs instead of rats and pancreatic juice instead of pancreatic tissue. Not only did he find variations in average relative enzyme concentration, possibly associated with change in diet, but he was unable to verify parallel secretion of enzymes in animals on a constant diet. Trypsin, amylase and lipase were determined daily. Considerable fluctuation in the concentration of each of these enzymes was observed from day to day. The variations in concentration of each enzyme were frequently unrelated to variations in concentration of other enzymes. (9)

Cellular source of secretion

Because the pancreas apparently possesses only one type of secreting cell it has been assumed that the fluid, bicarbonate and enzymes were all produced by the same type of cell. Recent work by Lagerlof and by Friedman and Snape has shown that in pancreatic disease the secretion of enzymes may be supressed, while the secretion of fluid remains normal or nearly so. This suggests that two different tissues may be involved in these functions. A study by Grossman and Ivy of the effects of alloxan on the pancreas suggests that the fluid may be secreted by the cells of the intralobular ducts. They found that in alloxan treated dogs in addition to the well-known damage to the islet tissue, the cells of the intralobular ducts showed vascuoliscation; at the same time there was a suppression of the secretion required to initiate secretion. Enzymes remained normal. In another study from Irv's laboratory it was found that pancreozymin, which increases the output of digestive enzymes from the pancreas, did not augment the output of alkaline phosphatase. Another observation made in the same study was that the phosphatase apparently was localized in the cells of the intralobular ducts, again implicating these ducts as being the source of certain constituents of the pancreatic juice. (4)

Until rather recently the most widely accepted theory concerning the regulation of pancreatic secretion was that of Mellanby who considered secretin as the regulator of water and bicarbonate secretion and vagal nerve impulses as the regulator of enzyme secretion. It was thought that the cooperation of these hormonal and nervous mechanisms accounted for all the fluctations in volume and composition of pancreatic secretion which ocurs in normal digestion. In 1943, another hormone was introduced into the picture. From studies of purified intestinal mucosal extracts, the actions of the two hormones have been clearly demonstrated to be as follows: secretin stimulates water and bicarbonate secretion while pancreozymin stimulates enzyme production. Now, two questions of primary importance remain to be answered: first, which foodstuffs, when present in the intestine stimulate the mucosa to release secretin in which to release pancreozymin: and second, what is the extent to which each of the two mechanisms, nervous and hormonal, contributes to the regulation of the external pancreatic secretion? Those questions have received different answers and the experiments of Wang and Grossman of the Department of Clinical Science, University of Illinois, try to answer the above two questions more quantitatively and defi-nitely. Dogs with a portion of the pancreas subcutaneously auto-transplanted were used for demonstrating the release of secretin and pancreozymin from the intestinal mucosa when various foodstuffs were introduced into the intestinal lumen.

(1) Distilled water has a weak stimulating effect on the transplanted pancreas while saline solution has none.

(2) HCL solution, when present in the small intestine acts as a powerful agent in the release of secretin, but also acts as a relatively weak stimulus for the release of pancreozymin.

(3) Products of protein digestion-peptone and amino acids solution are powerful stimuli for enzyme secretion by the pancreas (Pancreozymin effect). Their secretin effect is also prominent being second only to HCL.

(4) Fat (corn oil) and soap (Na oleate) are both effective in the stimulation of the transplanted pancreas and have a prolonged action. Soap is the more effective in the release of hormones, being second only to th protein group.

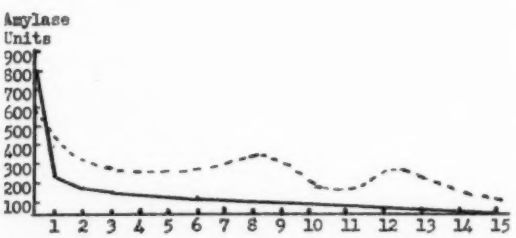
(5) Carbohydrates (soluble starch, maltose and dextrose) when present in the small intestine are not adequate stimuli for the pancreas under the conditions of this experiment.

(6) Atropinization does not abolish the effect of peptone acting on the pancreas indicating that a cholinergic nervous mechanism is not likely to be involved in the release of secretin and pancreozymin by various foodstuffs under the ex-

perimental conditions used. These experiments were performed using the subcutaneous autotransplanted pancreas in order to determine whether nervous connections between the intestine and the pancreas were necessary for the stimulation of enzyme secretion. (13)

Wang and Grossman of the University of Illinois College of Medicine reported an interesting paper on the "EFFECTS OF LIGATION OF THE PANCREATIC DUCT UPON THE ACTION OF SECRETIN AND PANCREOZYMIN IN RABBITS WITH A CORELATED HISTOLOGICAL STUDY." We have seen that secretin acts as stimulus for increasing the volume rate of pancreatic juice secretion and pancreozymin for enzyme output of the pancreas. The effect of ligation of the pancreatic duct upon the action of secretin and pancreozymin in response to a change in the pancreas, both histologically and functionally.

The following graph summarizes their findings:



Both the volume and the enzyme output of the juice showed a slow and gradual decrease from the low value obtained at 4 days to zero by the end of two weeks. After two weeks it is interesting to note that there is no amylase at all. The corresponding histological sections from the animals during this period showed that a gradually progressive degenerative process was taking place in the acinar cells. The infiltration of the fibrous tissue and the round cells became more pronounced as the ligation time increased and finally, at the end of two weeks, almost all of the acinar cells were associated with hyperplasia and enlargement of the ductules.

This resulted in a few dilated ductules surrounded by infiltrated fibrous tissue remaining in each of the lobules. If a longer period of ligation takes place, we have a gradual replacement of the acinar cells by the ductules with an atrophy of the lobules. The action of a single supramaximal dose of secretin and the action of pancreozymin gave approximately the same curve. The loss of function after different durations of ligation was correlated closely with the picture of degeneration of the cells as revealed histologically. Obstruction is believed to play an important role in the pathogenesis of pancreatitis. The present study permits an evaluation of the pancreatic changes produced by obstruction alone, without the additional factors of excessive stimulation of secretin and vascular impairment which are required to cooperate with obstruction if edema and necrosis of the glands are to occur. In clinical practice, when secretin is used to test pancreatic function it is usually found that the volume and bicarbonate show abnormally low values in early cases of chronic pancreatitis and only at a later stage is the enzyme output reduced. This suggests that the type of damage occurring in these clinical cases is different from that produced by obstruction of the ducts in the experimental animal. When pancreozymin becomes available for clinical use, it may help to clarify this apparent disassociation of function. (14)

Conditions in which pancreatic insufficiency occur clinically.

Derangement of pancreatic physiology is present in all forms of acute and chronic pancreatitis whether or not we are capable of detecting a change in functional capacity of the organ. Probably the severest form of insufficiency is seen in cases of pancreatic fistula, particularly where the tract connects with a large duct. Both true and pseudo cysts of the pancreas may be associated with severe disturbances in pancreatic function. Tuberculosis and syphilis represent rare causes of diminished activity. A wide variety of extra pancreatic conditions capable of producing secondary inflammatory changes in the pancreas will also cause a derangement of pancreatic physiology. (5)

Effcts of excluding pancreatic juice from the intestinal tract

The clinical or experimental picture obtained will depend upon whether the exclusion of pancreatic juice from the intestinal tract is complete or incomplete and whether or not this effect is produced by carefully ligating all connections between the pancreas and duodenum or by such a procedure plus the creation of a fistulous tract permitting the pancreatic juices to drain externally. The complete absence of pancreatic juice is probably never seen clinically, so that the full fledged syndrome may be best considered in the light of experimental evidence. When no pancre-

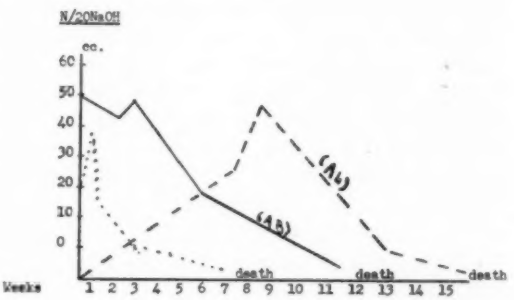
atic juice is allowed to enter the intestinal tract, there follow polyphagia, a gradual loss of weight, and the passage of large bulky, foamy stools containing undigested and unabsorbed fat and carbohydrate. Both Ivy and McClure attribute the polyphagia to an increased gastrointestinal motility and to a partial starvation secondary to defective intestinal digestion and absorption. The passage of bulky diarrheic stools appears early and seems to be directly dependent upon the amount of unabsorbed fat (steatorrhea) and unabsorbed protein (creatorrhea).

In the human being, the few cases described of complete external fistula gave the following syndrome: extreme anorexia, nausea, vomiting, profound asthenia, marked dehydration and rapid lossof weight; profound metabolic changes accompany the clinical symptoms and include progressive anhydremia, acidosis, a marked preagonal elevation of blood urea nitrogen and a decrease in blood plasma chlorides. In incomplete fistulae, the syndrome produced is like that of a complete external fistula, only perhaps less severe. (5)

Value of serum amylase and lipase determinations in the diagnosis of pancreatic lesions

Any mechanism which tends to block the normal egress of pancreatic juice from the main pancreatic duct into the duodenum may be reflected in an elevation of the serum amylase and lipase. We have no practical test for estimating trypsin in the blood. What are the mechanisms that would cause a complete or partial block of the main pancreatic duct? (1) Pancreatic stones or inspissated intraluminal contents; (2) intramural swellings due to inflammation or tumor of the main pancreatic duct; (3) extra luminal pressure on the main pancreatic duct in most instances due to inflamation or tumor, either in or adjacent to the pancreas. Elevated serum lipase and amylase values merely reflect the fact of increased intraluminal pancreatic duct pressure without reference to what might be the primary cause in the pancreas itself. The normal value of the serum lipase test are below 1.00 cc. of twentieth-normal sodium hydroxide, using the modified Cherry and Crandall technic. The serum lipase test requires a twenty-four hour period of incubation before completion. The serum amylase test may be reported within an hour. The normal values of the serum amylase test using the Somogyi technic are below 125 mg. of glucose. As with serum lipase, low values cannot be regarded as evidence of decreased pancreatic function. In acute pancreatitis the serum amylase values are more labile and seem to reflect rapid changes in the disease process to a more satisfactory degree than does serum lipase. In the more prolonged block of the main pancreatic duct seen in carcinoma of the head of the pancreas, the serum lipase is the more satisfactory of the two tests.

The following graph demonstrates a number of important aspects of the interpretation of the serum lipase in instances of carcinoma of the pancreas:



As with inflamatory changes in the head of the pancreas, the elevated serum lipase value is related to pressure on the main pancreatic duct but due in this instance to the influence of a growing tumor in juxtaposition to the main pancreatic duct. In case A.B. (solid line) the initial value of 5.0 cc. N/20 sodium hydroxide gradually fell to within the normal range of less than 1.0 cc. at the time of death. At necropsy almost the entire pancreas had been replaced by tumor tissue which was reflected in decreased serum lipase determination shortly before death in such a case gives an erroneous concept of the nature of the disease process. In a series of cases of carcinoma of the pancreas, an elevated serum lipase value will be obtained in only 40 per cent of the cases, due largely to the fact that the case is already in an advanced stage at the time of the initial admission to the hospital. Case A. L. (broken line) was picked up with an initial normal serum lipase value at a time when they were doing serum lipase determinations on all out patients merely to determine the specificity of the test in pancreatic cases. At operation and at necropsy, the diagnosis of carcinoma of the pancreas was established. In this case, we can follow the serum lipase from a time prior to compression of the main pancreatic duct, through the period of compression on the duct in the

presence of functioning pancreatic tissue and its final phase in which complete replacement of functioning pancreatic tissue by adenocarcimona was reflected in a serum lipase value within normal range about ten days prior to death. (9)

Lipocaic-deficiency syndrome

We will now see the most controversial question about the physiology of the pancreas: Dragstedt's lipocaic or Chaikoff's antifatty liver factor. The conception that lipocaic is an internal secretion of the pancreas depends on the recognition that the depancreatized dog fed on a mixed diet of protein, carbohydrate and fat is not restored to a normal state by the adequate administration of insulin and pancreatic juice, and that the remaining deficiency is corrected by oral administration of pancreas or of certain extracts of pancreas but not of other organs. Moreover the same workers found no changes in blood or liver fat in dogs with experimentally produced pancreatic fistulae. Therefore, they suggest that the alpha cells of the pancreas may function to produce the effective material.

On the other hand, pancreatic atrophy without diabetes and without histologic changes within the islands of Langerhans has been attended by marked fatty infiltration of the liver and an alteration of blood lipids. This leads to the conclusion that the acinar cells play a part in the secretion of lipocaic. Moreover, it has been shown by Montgomery, Chaikoff and their associates that the intestinal tract along with the endrocrine secretion of the pancreas and that the blood and liver lipids of duct ligated animals behave similarly, in every respect, to those of depancreatized animals.

The term lipocaic-deficiency syndrome may be applied to the phenomenon of fatty liver occurring in pancreatic insufficiency, a condition clinically and experimentally recognized for a number of years. How and why such pancreatic lesions cause secondary hepatic disturbances is not as yet quite clear. However, all observers agree that the pancreas secretes some substance necessary for the metoblism of fat in the liver and for its transport through the blood. (5)

Dragsted and his associates were first to make an alcoholic extract of the pancreas capable of preventing these changes. Later, they showed that the active material to which they gave the name of lipocaic, to be fat free, water soluble and almost entirely free of choline. Here are now the statements made by each school on this subject.

Dragsted's Statement. The demonstration that lipocaic is an internal secretion of the pancreas depends on the recognition that the depancreatized dog, fed on a mixed diet of protein, carbohydrate and fat is not restored to a normal state by the adequate administration of insulin and pancreatic juice and that the remaining deficiency is corrected by the oral administration of the pancreas but not by other organs. Extracts of pancreas have been prepared which are effective on oral and subcutaneous administration in daily doses of from 60 to 100 mg. of dried substance. Since these extracts are practically free from lecithin and choline, the former conclusion that the beneficial effect of pancras feeding in depancreatized dogs cannot be accounted for on the basis of its content of these chemicals is confirmed.

Experimental studies have demonstrated that the oral administration of fresh active pancreatic juice, with insulin therapy, does not prolong life or prevent the characteristic fatty changes in the liver, although the digestion and absorption of food are much improved. (15)

Chaikoff's statement. There can be no doubt that the pancreas contains a factor other than insulin that prevents the deposition of excessive amounts of fat in the liver. Evidence for this view was first obtained in the completely depancreatized dog kept alive with insulin in which fatty livers were found to develop when the animal was maintained on a diet adequate in proteins, vitamins and salt but lacking raw pancras. Later work showed that ligation of the pancreatic ducts was sufficient to induce fatty livers. The question now arises as to how the factor in the pancreas that inhibits the accumulation of excessive amounts of fat in the liver is made available to the organism. Although observations on the duct ligated pancreas suggest that the factor is released by the external secretion of the pancreas, the fact must not be overlooked that this procedure is associated with atrophy of a portion of the gland and hence may be responsible for the destruction of an internal secretory mechanism. That unequivocal evidence for the action of the external secretion could be obtained only by directly examining the effects of the digestion of pancreatic juice upon lipid metabolism. This has been done in the present investigation. Conclusive evidence is given that fatty livers pro-

duced either by excision of the pancreas or by duct ligation can be completely prevented by the daily ingestion of pancreatic juice.

The mechanism whereby pancreatic juice brings about this effect is at present obscure. Absorption of the liver factor probably occurs after the pancreatic juice is poured into the small intestine, but an answer to the question whether it is absorbed unaltered in the form present in the pancreatic juice or whether before absorption it is changed by an interaction with the intestinal mucosa or some dietary constituent must await further investigation. Irrespective of these speculations, it is now apparent that the evidence provided by Dragstedt and his coworkers for the claim that the liver factor is released by the pancreas by way of the blood stream only and not through the external secretion of the gland is no longer tenable. (16)

These contrary results and conclusions have not yet been resolved. What concerns us however, is the area of agreement, i.e., that the pancreas secretes whether internally or externally, a lipotrophic agent other than choline.

For practical reasons of simplifying experimental procedures and permitting the use of large number of animals, much work has been done with the rat which readily develops a fatty liver when maintained on a diet deficient in choline or choline precursors. Best and his co-workers (17 & 18) have claimed that in such animals, pancreatic extracts have no effect beyond that which can be accounted for by the choline content of the extracts. On this basis, these workers doubt the existence of any other lipotrophic factor originating in the pancreas. However, this conclusion is hardly warranted by the observations.

If, as is outlined, Dragstedt's lipocaic and/or Chaikoff's anti-fatty liver factor acts by liberating the choline precursor (methionine) from the foodstuffs in the gastrointestinal tract, it is obvious that such pancreatic extracts cannot be effective when the foodstuffs in the gastrointestinal tract are deficient in the choline precursor. If, as has been suggested, "lipocaic" acts by catalizing the liberation of free methionine from the products of protein digestion in the gastro-intestinal tract or by facilitating the absorption of methionine, it is obvious that its effect will be conditioned by the amount of protein in the diet and the adequacy of the digestive enzymes. Work in progress by Haanes and Gyorgy is strongly in favor of the proteolytic nature of the active lipotrophic fraction of the pancreas. They have shown that a potent fraction of pancreas which is lipotrophic when given by mouth to depancreatized dog exhibits the characteristic action of a trypsin-like enzyme, which may be masked by the simultaneous presence of trypsin-inhibitor. However, duodenal juice inactivates the inhibitor. The active factor is capable of liberating methionine from a pepsin digest of casein.

Then, in the depancreatized animal, we can attempt to analyze the situation by pointing out that it suffers from three separate deficiencies: (1) lack of insulin (2) a lack of pancreatic digestive enzymes and (3) a lack of pancreatic factor, Dragstedt's lipocaic or Chaikoff's antifatty liver factor. Each deficiency has its own characteristic syndrome; but each influences the manifestations of the other deficiencies when they exist together: (1) Lack of insulin, this has nothing to do with the present paper. (2) Lack of pancreatic digestive enzymes: interferes with complete digestion of all the proteins in food. This partly accounts for the chronic weight loss and negative nitrogen balance despite the use of adequate amounts of insulin. It also provides insufficient amounts of methionine not only for the synthesis of body protein but also the manufacture of choline. This together with the lack of "lipocaic", leads to a fatty liver and liver dysfunction, as evidenced by a rise in the serum alkaline phosphatase and a drop in the serum cholesterol esters. The animal has no difficulty in making choline from methionine but his difficulty is in liberating or absorbing free methonine. If lipocaic acts by catalizing the liberation of free methionine from the products of protein digestion in the gastrointestinal tract or by facilitating the absorption of methionine, its action will be partly dependent upon the completeness of protein digstion. Even if the liberation or absorption of methionine is not catalyzed by lipocaic, these processes may be assumed to proceed at some suboptimal rate. Thus the purely digestive action of pancreatic juice may partly account for the favorable effects of feeding it to depancreatized dogs, without the necessity for supposing that pancreatic juice contains "lipocaic." (20) (3) Lack of lipocaic: has been described above.

As you can see, the discussion remains open on this interesting but controversial subject of "lipocaic."

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PHOENIX *Clinical* CLUB

MASSACHUSETTS GENERAL HOSPITAL CASE NO. 36341

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A fifty-five-year-old man was admitted to the hospital because of malaise, fever and progressive generalized weakness.

The patient was well until five weeks before entry, when insidiously he began to feel tired, lost his appetite and noted generalized weakness. However, he continued to work until three weeks before entry, when he developed chills with fever and the weakness became worse. A doctor gave him twenty doses of aureomycin and ten injections of penicillin. The weakness increased slowly and was accompanied by tenderness of both thighs. The temperature continued elevated, running from 100 to 102°F. Ten days before admission he began to vomit and had some diarrhea, both of which persisted. Four days before entry he became afebrile, and the penicillin was discontinued. Two days later because of persistent vomiting he was given several doses of tincture of belladonna, and a maculopapular rash appeared on the neck, face, chest and trunk. Despite increasing weakness he was able to walk with assistance until the morning of admission, when suddenly he could barely move his legs.

The past and family histories were irrelevant.

Physical examination revealed an acutely ill man with frequent hiccuping. The skin was very dry, with a maculopapular rash and a few pustules on the face, neck and trunk. The conjunctivas were injected, and the fundi clear. The tongue was parched, and there was bleeding of the palate. The pharynx was dry and injected, without exudate. The lungs were clear. The heart was not enlarged. The sounds were distant; there was sinus rhythm at a rate of 88, with a Grade I apical systolic murmur. The abdomen was soft, with no masses or tenderness. Rectal examination was negative. Neurologic examination revealed profound generalized weakness. The cranial nerves were intact, and no sensory changes were found. The ankle and knee jerks were absent, and the biceps and triceps hypoactive.

The temperature was 100°F., the pulse 90, and the respirations 22. The blood pressure was 140 systolic, 90 diastolic.

Examination of the blood disclosed a white-cell count of 17,700, with 78 per cent neutrophils. The nonprotein nitrogen was 310 mg., the total protein 3.5 gm., the fasting blood sugar 207 mg., the phosphorus 19.9 mg. and the calcium 8.1 mg. per 100 cc., and the sodium 135.6 milliequiv., the choloride 97 milliequiv., and the potassium 10.1 milliequiv. per liter. A blood culture was negative. An X-ray film of the chest was not remarkable. An electrocardiogram showed a normal rhythm, with a PR interval of 0.32 second. The QRS complexes were wide, with a duration of 0.14 second and bizarre configuration. The T waves were high and peaked and ST segment depressed in Leads V2 through V6. The electrocardiagram was considered consistent with potassium intoxication. A lumbar puncture taken just after admission revealed a clear colorless fluid under an initial pressure equivalent to 140 mm. of water and a final pressure equivalent to

80 mm. of water. The spinal fluid contained 4 red cells per cubic millimeter. The gold-sol and Wassermann tests were negative.

On admission the patient was given 5 per cent dextrose in physiologic saline solution intravenously. After receiving 700 cc. he recovered muscular function, and the reflexes were normal. During the next twenty-four hours he received 5500 cc. of 5 per cent dextrose in physiologic saline solution. However, he continued to be markedly dehydrated, vomited moderate amounts of bile-stained fluid and passed no urine. On the second hospital day he appeared drowsy, and the rash became more extensive. Physical examination was essentially unchanged except for hypoactive reflexes. Trousseau and Chvostek signs were negative. The nonprotein nitrogen was 340 mg., and the fasting blood sugar 207 mg. per 100 cc., and the potassium 8.7 milliequiv., the chloride 103 milliquiv., and the carbon dioxide 10.1 milliequiv. per liter. The electrocardiogram was almost normal with normal PR intervals and QRS complexes. The T waves were low in Leads 1 and AVL and normal in the other leads. The hemoglobin was 9.5 gm. per 100 cc., and the white cell count was 12,500. A cystoscopic examination was performed, with catheterization of the left ureter; aspiration yielded a white, milky material followed by 10 cc. of urine, which contained many red cells, white cells and casts. The retrograde pyelogram showed a normal left kidney. The right ureter could not be catheterized because of movement of the patient. Because of the persistent anuria, he was put on the artificial kidney, with a blood flow averaging 300 cc. per minute. At the beginning of the procedue the nonprotein nitrogen was 220 mg., and uric acid 10.5 mg., the creatinine 29.2 mg., and the blood urea nitrogen 153 mg. per 100 cc., and the carbon dioxide 8.3 milliequiv., the sodium 139.5 milliequiv., the chloride 107 milliequiv., and the potassium 8.3 milliequiv. per liter. During the procedure he became unresponsive and had a slight hypertensive effect. The dialysis was continued for six hours. After dialysis, the nonprotein nitrogen was 160 mg., and the blood urea nitrogen 147 mg. per 100 cc., and the carbon dioxide 13.4 milliequiv., the sodium 146.6 milliequiv., the chloride 113 milliequiv., and the potassium 4.5 milliequiv. per lter. Shortly thereafter he developed marked laryngeal stridor requiring intubation, which established a good airway. Gradually he lapsed into deep coma and died sixty hours after admission.

DR. BEN P. FRISSELL

This 55-year-old man presented himself at the time of his hospital entry with classical symptoms and signs of terminal renal failure, or uremia. Practically all of the symptoms which he presented would appear to fit into the protean symptomatology of this condition. Likewise, the accumulated laboratory data, including the extremely high non-protein nitrogen (310 mgm. on admission) and the low total blood protein, (3.5 gm.) the high phosphorus level 19.9 mg. (as compared to a normal of 9-11), and the potassium level of 10.1 milliequiv. which would be considered as a high level for this particular electrolyte, and the apparent anemia as evidenced by hemoglobin of 9.5 gms. are in keeping with uremia. The EKG changes of uremia are variable and are interpreted usually as taking on the elements of changes in electrolyte balance of the blood as well as organic changes in the myocardium. Fasting blood sugar of 207 mg. recorded on two occasions is not a usual finding in uremia, but in an anuric patient, such as the one in question, an elevated blood sugar would certainly be expected after the use of intravenous dextrose which he had on admission and apparently continuously for at least 24 hours to the tune of 5,500 cc. which should certainly be enough not only to raise the blood sugar but to kill a patient already in the terminal stages of renal failure with anuria very likely due to so-called "lower nephron syndrome." It is a marvel that he lived for 60 hours after admission, even long enough to be subjected to the use of an artificial kidney.

Our understanding of uremia has improved considerably during the past decade or so, but after carefully perusing the current literature, one cannot help but realize how little we actually know about renal function, particularly pathological renal function. Nonetheless, a great deal of improvement in our understanding of the situation has come about by the simplified classification of renal disease as advanced by Bell and others who have been active in this field of endeavor. Th term "uremia" originally chosen to designate a syndrome associated with nitrogen retention in the blood is much too simple to cover the complicated changes which occur in the electrolyte balance of the blood as a result of renal failure. The symptom complex is likewise extremely complicated depending largely upon the

status of electrolyte balance. For instance, there may be marked edema associated with sodium retention or there may be severe dehydration as in our case with low or normal sodium levels in the blood. Potassium may be either high or low as may be the case with calcium, phosphorus, etc. There is practically always a low carbon dioxide combining power as was in our case with resultant acidosis. The urine output may sometimes be increased or the patient may be completely anuric.

Our problem would appear to be that of attempting to arrive at a reasonable explanation for the rapid progress of this man's disease. We have a man who apparently was well five weeks, or a little longer, before his final demise and whose original symptoms did not suggest renal disease but rather pointed to some systemic infection. The fact that his past history does not give any evidence of renal disease does not rule out the possibility of pre-existing renal damage. After all, the man was 55 years old and could have had considerable renal involvement on an arteriosclerotic basis, a condition which is notably insidious and benign in its progression. Likewise, glomerular nephritis is many times discovered in an advanced chronic stage without any evidence of an initial acute attack which is generally conceded to be the precursor of a chronic nephritis of this type. According to Bell's series, he was able to obtain a history of an acute nephritis in only 54 cases whereas 213 cases, no pre-existing renal pathology was known to the patient.

In attempting to arrive at a diagnosis, I have considered the various causes of uremia. For the purpose of differential diagnosis, Barnes, in a recent article in the JAMA, has classified uremia into two large groups: (A) The obstructive bilateral lesions, or the so-called "urological uremias" and (B) The non-obstructive bilateral renal lesions, or the so-called "medical type" of uremia. The latter group has been further classified by Pruett of Mayo Clinic into (a) Glomerular lesions, (b) Primary vascular lesions, (c) Tubular lesions, (d) chronic diffuse nephritis and (e) Secondary renal failure, or so-called prerenal azotemia.

(A) I believe the obstructive group needs only casual perusal to rule them out. This group includes prostatic hypertrophy, cancer of the bladder and lower urinary tract. The course in this type of uremia is usually insidious, indolent in character. There is usually not a marked increase in NPN in comparision to the non-obstructive type. They are usually non-ferbile except for complicating urinary tract infections. What little X-ray evidence we have in this case does not point to any obstructive lesion.

(B) Of the Non-obstructive group: (a) Glomerular lesions are perhaps the best known and will be considered first. Of this group, (1) glomerular nephritis heads the list. This disease is characteristically a disease of young people occuring usually before the age of 10 years. The clinical course of the acute form of this disease does not parallel the symptoms present in our case. The so-called triad of symptoms, *hypertension, edema,* and *renal insufficiency* is not fulfilled in our case. There is usually grossly bloody urine in the acute stage of the illness, fever usually lasts for not more than a week, kidney involvement is usually preceded by streptococcic infection of the upper respiratory tract. In 90 per cent of the cases in children the course results in complete recovery and in adults where there has previously been a damaged kidney by previous involvement, the condition tends to lapse into a more chronic form of nephritis gradually terminating in uremia. (2) *Kimmelstiel-Wilson's disease,* so-called intercapillary glomerulosclerosis, first described by the above investigators in 1936, is a nephritic syndrome seen frequently in diabetic patients, usually past middle life, the primary lesions occurring in the glomerular portions of the kidneys. These changes are very closely tied up to those found in arteriosclerotic kidney disease, and, although they are sometimes found without diabetes, usually are found in conjunction with it; according to Bell's series, occurring in 25% of necropsy cases of diabetics. The course is not usually acute. Hypertension is the rule in these cases. No hypertension was noted in our case and even though we are confronted with the blood sugar slightly elevated, I do not believe that the above syndrome is the answer to our problem. (3) *Amyloid disease.* Another glomerular condition to be considered is so-called amyloid disease of the kidney, "amyloid nephrosis" as it formerly was called with its characteristic picture of edema, albuminuria, and hypoproteinemia. This condition presupposes amyloid disease which is not evidenced in our case. (4) Disseminated lupus erythematosus, another condition, (a rare one which makes it a good bet for our Club) which is said to involve primarily

the glomerular structure of the kidney in those cases in which renal complications are found during the course of the disease. It was formerly believed that the changes in this condition were characteristic of the disease but more recent investigation has indicated that the lesion is merely a mild form of acute glomerular nephritis or glomerulitis. It is very seldom found to develop into a severe degree of kidney disease and the renal lesions can be considered fairly benign in comparison to the picture we are facing in our present case.

(b) Primary vascular disease of the kidney includes so-called (1) arteriosclerotic kidneys of the senile type, (2) diffuse arterial disease under the classification of essential hypertension, and (3) perarteritis nodosa. In all of these instances, hypertension is the outstanding symptom. The course of the disease is more insidious than that under consideration today.

(c) Tubular lesions. This group of renal lesions has been reduced to rather simple proportions during the past decade. Bell distinguishes two types of tubular disease; the so-called *degenerative* and the *obstructive* lesions. The degenerative lesions include chemical poisoning such as mercuric chloride, carbon tetrachloride, uranium nitrate. Obstructive lesions include the syndrome produced in sulfonamide poisoning and the reactions to incompatible blood transfusions and the renal complications accompanying multiple myeloma. Mixed type of involvement of the tubular structure, namely, a combination of both the degenerative and the obstructive lesions, probably occurs in all of these situations mentioned above. This is of course the category of renal disease which has recently come to be known as so-called lower nephron syndrome, or "acute renal insufficiency" in its more acute form. Clinical features are usually anuria, oliguria, azotemia, hypertension, and uremia. The mechanism of damage to the tubular structure of the kidney is still not clearly understood but an ever increasing list of possible causes has come to be considered from an etiological standpoint. A recent paper by Thomas W. Parken gives the following conditions which may initiate so-called lower nephron syndrome: (1) Prolonged shock, (2) Congestive heart failure, (3) Acute pyelonephritis, (4) Overdose of, and sensitivity to, sulfonamides, (5) Intravascular hemolysis, (6) Poisoning by heavy metals, (7) Severe burns, (8) Crush injury syndrome, (9) Extrarenal obstructive lesions of the genitourinary tract, (10) Dehydration and loss of inorganic bases, (so-called extrarenal uremia) (1)) Acute glomerular nephritis, (12) Toxemia of pregnancy, (13) Intoxication by noxious chemical agents, (14) Certain urological procedures, (15) Postoperative suppression of urine, (16) Septic abortion, (17) Blackwater fever, (18) Cholera, (19) Yellow fever, (20) Weil's disease, (21) Hepatic failure, and (22) Heat stroke. Certainly, from the list of factors given above that may cause this syndrome, it is obvious that no single pathological process can be expected at autopsy. On the other hand, it does appear from clinical evidence accumulating from time to time, that changes in the tubular structure of the kidney, whatever the nature and the origin, are somehow responsible for the altered renal function.

(d) To proceed with further consideration of non-obstructive bilateral renal lesions, chronic diffuse nephritis and secondary renal failure or so-called prerenal azotemia remain to be discussed. It is found, however, that various conditions producing so-called "prerenal azotemia" are included in Parken's "acute renal insufficiency"; namely, congestive heart failure with its resultant functional renal ischemia, and prolonged shock such as may be produced from severe burns, crushing injury, surgical procedures, massive hemorrhage, and Addison's disease. The mechanism in these instances is renal hypotension and, lastly, dehydration with its resultant dimunition in the amount of blood flow through the kidneys. It is doubtful if any of these conditions are present in the case in question. They usually run a relatively mild course as far as renal failure is concerned and are capable of responding to appopriate therapy.

(e) There remains for discussion the so-called group of "chronic diffuse nephritis." This term is an outgrowth of the former terminology, interstitial nephritis, and includes pyelonephritis, bilateral hydronephrosis, polycystic disease of the kidney and leukemic or lymphoblastic infiltrations of the kidneys. Pyelonephritis exists both in an acute and chronic form. Bell makes a very concise and illuminating statement about this group of renal diseases when he states that the most important feature of this type of renal disease is that "it is caused by the lodgement of bacteria in the kidneys." This in contradistinction to glomerular nephritis where bacterial toxins, or sensitivities to bacterial products are apparent-

ly responsible for the kidney changes rather than the actual inflammatory reaction due to bacterial invasion. This reaction may be disseminated throughout the structure of both kidneys and, as the name implies, involves all structures of the kidney rather than any one isolated portion of the nephron. The acute stage of pyelonephritis is characterized by chills and fever, sometimes no localizing symptoms pointing to the urinary tract. Pyuria which develops after a few days may not be present in an early specimen of urine. Nausea and vomiting may be commonly found. Leukocytosis may be in the neighborhood of 15,000 to 20,000. The acute symptoms usually subside in a period of five to seven days or may progress to the stage of chronic pyelonephritis or may develop into acute renal failure. Certainly the initial symptoms in our case could fit the category of an acute pyelonephritis. Under ordinary circumstances, one would expect that treatment with penicillin and aureomycin would favorably influence the course of this disease. However, under conditions of present day medical management, it is quite possible for even the ordinary organisms found in these lesions to have become drug-fast to any of the various anti-biotics and chemotherapeutic agents. And, furthermore, it is not beyond the realm of probability that our esteemed judge might have failed to disclose the fact that other therapeutic agents might hav been utilized in this case. (I am referring, of course, to Dr. Dysart and the drug, a sulfonamide).

The finding of an apical systolic murmur, I believe, is likely of no significance other than being a terminal issue in a dilated heart accompanied by a severe degree of anemia. However, this suggests the possibility of *subacute bacterial endocarditis* which may be a factor in the production of metastatic renal lesions of the type described above.

Typhoid fever has been known to produce a severe degree on pyelonephritis in its terminal stages. In this instance, the time is short for such development. The typical blood picture is not in evidence. *Weil's disease* not infrequently produces acute renal failure with the pathological picture approaching that of lower nephron syndrome. The onset of this disease is usually very abrupt which is at variance with our case. 70% of the cases show definite jaundice and hepatic involvement as a primary pathological process. There is no hint in the present case that liver pathology exists. The skin rash which is present as described in our case, could, of course, be due to Weil's disease or could likewise be explained on the basis of uremia which I am inclind to believe is the case. *Polycystic* disease of the kidneys should perhaps be mentioned in passing. The brief duration of the symptoms, the absence of X-ray findings, etc., are against this diagnosis. The infiltration of the kidney structure by leukemic or lymphoblastic cells or, in fact, by any metastatic malignant growth may produce symptoms of renal failure. These gradually produce the symptoms characteristic of so-called chronic diffuse nephritis. There may be hypertension, edema may or may not be present, albuminuria, and gradual development of chronic uremia.

In conclusion, I am inclined to believe that our patient died of so-called acute renal failure, otherwise termed "lower nephron syndrome." Of the causative factors, I believe that most likely we are dealing with acute *pyelonephritis* complicated perhaps by sulfonamide treatment and resultant toxic reactions to this drug.

DR. LOUIS B. BALDWIN

At the time this 55 year old man was admitted to the hospital, the blood studies revealed a profound uremia and it is left for us to determine the underlying disease. The symptoms fit in well with this diagnosis. There was hiccuping. The skin was dry with a maculopapular rash and a few pustules on the face, neck and trunk. There was profound generalized weakness and the pharynx was dry and injected. The blood pressure was only slightly elevated, and in view of the normal occular fundi had not previously been elevated for a long-period of time. It is to be assumed that, at the time of his admission, there was a total anuria, for there is no record of a urinalysis, and only a small amount of urine was obtained at cystoscopy from the left ureter. This yielded a milky material followed by 10 cc of urine, which contained many pus cells, red cells and casts. The left kidney appeared normal by retrograde pyelogram.

The cause of uremia may be either bilateral obstruction to urinary outflow, or non-obstructive bilateral renal disease. But it must also be kept in mind that neither of these conditions may be the cause of lower nephron nephrosis produced by shock and other causes, the underlining condition is one of impaired volume flow of blood

through the kidneys, and relative concentration of the blood.

Let us consider renal disease first. We have a 55 year old man, who was presumably well until five weeks before admission to the hospital. He then noted lassitude, weakness and loss of appetite. But he apparently had no pain, nor other symptoms pointing to urinary obstruction. From the cystoscopic examination we may rule out polycystic renal disease.

If there were an obstruction of the vesicle orifice or urethra, there would be dysuria, frequency and urgency are bladder distention. It is extremely unlikely, therefore, that he had an enlarged prostate or other bladder obstruction to account for the uremia. Bilateral ureteral involvement fom calculi or neoplasm would almost invariably cause lumbar pain referred to the groin. The bilateral tenderness of both thighs complained of by this patient might be on the basis of weakness, it might also be due to renal calculi. Had there been renal or ureteral calculi in both sides, one would expect the retrograde left pyelogram to reveal this fact. The evidence that is given to us is therefore against the diagnosis of post renal obstruction to account for the uremia in this case.

Chronic glomerular nephritis is a common cause of uremia. In this disease, the vast majority of cases begin with an insidious onset and the discovery is often made by accident in the course of a routine examination. In a series of 80 patients reported by Bradley and Loeb the observed duration of this disease varied from a few months to more than forty years. Of this group 18 per cent lived less than a year after the establishment of the diagnosis.

Weakness, lassitude, and loss of weight are probably the most common complaints in chronic nephritis. In about 10 per cent the course is utterly devoid of symptoms up to the stage when the symptoms of terminal uremia develop. In some cases a latent nephritis may become active, particularly in association with streptococcal infection. After a recrudescence of this type, the disease may again become quiescent only to flare up again at some subsequent time. Hypertension may be absent in chronic nephritis and only moderately elevated as a terminal event. In those cases that do not have hypertension, retinal changes almost never occur.

In the present incidence there was a brief illness of only 5 weeks duration. From what has been said about chronic nephritis, it might be assumed that the patient had a latent chronic nephritis which entered the terminal stage of uremia at the time he began feeling ill. In favor of this view is the anemia (9.5 gm. hemoglobin per cent) which always accompanies a long lasting nephritis and the blood changes characteristic of uremia. Moreover, the urine contained many red cells and casts. The total blood protein was about half the normal, the blood calcium was low, but the sodium and chloride were only slightly depressed, whereas, the potassium was 10.1 per cent, which is double the normal value. The phosphorous of the blood was extremely high and there was a marked acidosis. The other findings were what might be expected in uremia, though the blood sugar was somewhat high, it might be explained in part by the glucose infusions that were given. It is interesting that the electrocardiogram was consistent with potassium intoxication.

What has been said about chronic glomerular nephritis might just as well apply to arteriolar nephrosclerosis, except that in this condition, there are more often retinal changes and hypertension.

Against the diagnosis of chronic nephritis are the fever and the pus in the urine, though both of these conditions may occur as complications of the disease.

In patients first observed when albuminuria and renal insufficiency are already present, the diagnosis is difficult and may be of great practical importance. For example, Butler has reported two cases in which pyelonephritis involving only one kidney has led to hypertension and the clinical picture of arteriolar nephrosclerosis. In these two patients removal of the diseased kidneys has resulted in cure.

Kidney infection must be seriously considered in this case, in spite of the fact that it is more often the cause of chronic renal disease in the female than the male. Two factors seem to be of particular importance in the susceptibility of the kidney to infection, these are calculus or obstruction to urinary flow. Congenital malformation in the calices, pelvis, or uterers often predisposes to infection of the urinary tract. Acute pyelonephritis or pyelitis should be suspected in patients with unexplained chills, fever and malaise. In some cases there may be repeated acute attacks without the characteristic lumbar pain or costovertebral tenderness. In patients suspected

of having Bright's disease because of albuminuria, pyelonephritis should be considered as a possibility when numerous white blood cells are also present in the urinary sediment. In these instances acute pyelonephritis may lead to wide spread suppuration of the kidney and if both kidneys are involved the patient may succumb to uremia. In the case under discussion this diagnosis seems untenable because of the normal left kidney seen by pyelography. Chronic bilateral pyelonephritis is more common in children and in women, but is by no means uncommon in older men. The pathological changes in the kidneys, according to Longcope, suggest that the progress of the disease is caused through the gradual destruction and diminution by inflammation and scarring of small portions of the kidney. The clinical picture is variable and at times the symptomatology is so mild and vague that the disease escapes detection until it is far advanced.

As can be seen from this description it is impossible to rule out the terminal stage of chronic bilateral pyelonephritis in this case. There are the pyuria, and chills and fever, there is also an anemia probably indicating a chronic process.

Other urinary infections such as tuberculosis seem extremely unlikely. In conclusion three conditions should be mentioned as capable of producing uremia. Acute hepatitis may terminate in uremia, though this case gives no history or signs of having had acute hepatitis. It may be argued that a lower nephron nephrosis was superimposed upon a pre-existing nephritis by antibiotic therapy. In a recent A.M.A. Journal, Spring reports purpura and nephritis after administration of procaine penicillin, and in the same Journal, Gittell reports a shock-like state resulted from the administration of aureomycin. It must be further noted that in about 10 per cent of cases of lower nephron nephrosis acute pyelitis or pyelonephritis occurs as a complication.

However, the marked anemia as shown by the low blood hemoglobin is against the diagnosis of lower nephron nephrosis in this case.

Finally diffuse renal periarteritis and lupus erythematosus may terminate in uremia but seem untenable diagnosis in this patient, as does amyloidosis. It is noted that the treatment with intravenous solutions in this case were entirely too energetic.

Final diagnosis:

1. Chronic pyelonephritis–uremia.
2. Lower nephron nephrosis.
3. Chronic glomerular nephritis with complicating renal infection.

DIFFERENTIAL DIAGNOSIS

Dr. Charles L. Short*: We might look at the X-ray films first, Dr. Wyman.

Dr. Stanley M. Wyman: The chest and heart and not remarkable. The films taken from the retrograde pyleogram show a normal-appearing left kidney, with normal calyxes and pelvis. The right kidney is poorly outlined but appears within normal limits in size and shape.

Dr. Short: There is not even a suggestion of a filling defect in the calyxes?

Dr. Wyman: Not that I can see.

Dr. Short: The chest shows no signs of a healed infection or pneumonia?

Dr. Wyman: I do not see anything to suggest any previous trouble.

Dr. Short: The story is essentially that of a ferbile illness that came on insidiously and gave no real localizing features except possibly the vomiting, the diarrhea and the tenderness of the thighs. The ferbile phase was apparently subsiding, perhaps in response to antibotics, shortly before admission. Simultaneously, the patient became much sicker and was found on admission to be in extreme renal failure, with anuria. At this time two features of potassium intoxication were apparent–namely, the severe muscular weakness and the electrocardiographic changes. The potassium intoxication responded rapidly to intraveneous administration of saline solution and glucose, but otherwise the patient failed to respond to treatment, which included a run with the artificial kidney. This was quite effective as far as the blood flow and the improvement in the blood chemical findings were concerned.

I think the first point we have to decide in this patient is whether the whole illness, including the terminal uremia, represented one disease or whether he died from renal failure secondary either to the febrile disease or to the treatment that was employed. I can think of only two or perhaps three ferbile diseases that commonly terminate in renal failure with anuria. The first is Weil's disease. One usually thinks of this condition as a form of hepatitis, but severe renal involvement is frequent and death may ensue from uremia. This diagnosis was suggested to me by the tenderness of the thighs, since muscle tenderness may be one of the most distressing features of this condition, surpassing that which is

*Associate physician, Massachusetts General Hospital.

Childhood constipation deserves treatment which gently restores normal peristaltic movements; drastic elimination cannot permanently correct the condition and may be harmful to the child.

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SEARLE Research in the Service of Medicine

found in trichoinosis. The injection of the conjunctivas and the rash are consistent with this diagnosis. I believe, however, that the absence of jaundice or of liver enlargement is sufficient to exclude Weil's disease in this patient. It is true that in many cases of Weil's disease, jaundice or signs pointing toward hepatitis may be entirely absent, but death in the absence of jaundice is certainly extremely rare.

The second febrile illness that may end in uremia is the severe form of pyelonephritis, which occurs more commonly in diabetes, usually called necrotizing renal papillitis. There is a record in this case of two fasting blood sugar determinations of over 200 mg. per 100 cc. That is fairly good evidence for diabetes. Necrotizing renal papillitis may come on insidiously, without localizing signs, and the diagnosis is often made only at autopsy unless the possibility is thought of in life. This usually appears in nondiabetic patients only with urinary obstruction, for which there was no real evidence in the case under discussion. There are two points against this diagnosis; the first is the disappearance of fever before admission, and probably much more important the normal retrograde pyelogram, at least of the left kidney. Since in the fatal cases the process is usually bilateral, I think we have to discard this diagnosis. On the other hand, if Dr. Wyman had shown us irregular filling defects of the renal calyxes I think I could have made the diagnosis with some assurance.

The third febrile illness that may terminate in this way is periarteritis nodosa in a rather acute fulminating form. There were no helpful diagnostic points that I can discover that would enable one to make a diagnosis of a primary or idiopathic periarteritis nodosa to explain the whole illness.

In going over the history it seemed to me more likely that the renal failure was secondary and not actually a part of the patient's disease for which he was given antibiotics. The history gives no clue to the original disease, although presumably it was an infection that had apparently responded to therapy. The vomiting and the diarrhea might have resulted from the aureomycin, although we are not told the exact time when this drug was administered. The question might be raised here of extrarenal azotemia secondary to vomiting and diarrhea. I do not believe that this is likely as the sole explanation of the renal failure unless he had pre-existing renal disease. Pre-existing Bright's disease is not suggested by the history although the low serum protein brings up the possibility of a chronic glomerulonephritis. The normal blood pressure, the lack of eyeground changes and the anuria are all against a terminal stage of glomerulonephritis.

It think it is more likely that this patient suffered a catastrophic insult to the kidneys in the form of lower-nephron neprosis or cortical necrosis. None of the known causes of lower-nephron nephrosis have been recorded in this case—shock, intravascular hemolysis or sulfonamide intoxication. I know of no evidence that toxicity from antibiotics such as penicillin or aureomycin may be responsible. He may have had a certain degree of shock from the vomiting and diarrhea, but I am reluctant to make this diagnosis without adequate causative factors. The most reasonable explanation of this man's death from renal failure would seem to lie in a severe reaction to one of the antibiotics given, with hypersensitivity as the probable mechanism. It is well known that allergic manifestations in the form of rashes have been recorded after aureomycin. The development of a rash in this patient and the renal failure occurring after the apparent subsidence of the original infection are the most important clues to the diagnosis that I wish to present—namely, hypersensitivity to penicillin or aureomycin, with vascular lesions resembling periarteritis nodosa and cortical necrosis of the kidney. I am reminded here of a patient* discussed at one of these conferences several years ago who died in severe renal failure consequent to sulfonamide toxicity and who showed at autopsy the findings I have just mentioned.

Dr. James J. Currens: I think it might be of some interest to know that the requisition for the electrocardiogram raised the question of low potassium because of the muscular weakness and paralysis, and the electrocardiographic evidence was really the first indication of serious potassium intoxication. That there was a rather dramatic change in the electrocardiograms within about eighteen hours after 2 or 3 liters of fluid had been administered, is important, I think, particularly since the serum potassium changed very little—from about 10 to almost 9 milliequiv. per liter. This helps corrobrate the evidence that we are collecting that there is no correlation between serum potassium levels and electrocardio-

*Case Records of the Massachusetts General Hospital (Case 28501). New Eng. J. Med. 227:922-927, 1942.

graphic changes. Also, the serum sodium was essentially the same on these two occasions so that the ratio of sodium to potassium was again about the same. It raises the question, which is as yet unanswered, whether intracellular potassium, particularly in the conduction system, is the important factor in this regard.

Dr. Lloyd H. Smith, Jr.: As the patient died six hours after being on the artificial kidney, I might make a brief comment about the procedure. It was a very satisfactory dialysis lasting about six hours; in fact, it was the most satisfactory dialysis from a technical standpoint that we have ever had. The bath with which he was dialyzed was modified in one important way. Because of the very high serum potassium level we omitted potassium from the dialyzing fluid. We thought the results would be correspondingly good and were very surprised and disappointed that he died in such a mysterious fashion soon after the dialysis.

Dr. Richard Goldsmith: Regarding what Dr. Currens said, I wonder if it might be assumed, in a man who was given 5500 cc. of fluids intraveneously, that there was a relapse of potassium from the cells to the blood that kept up the serum potassium concntrate?

Dr. Marian Ropes: At the time of admission this patient presented a very confusing picture. Clinically, there was little to suggest renal failure. He was extremely clear mentally. We ascribed the anuria, which was apparent a few hours following admission, to the extreme dehydration. We believed that he had an infections disease resulting in this condition of almost complete paralysis and of heart block. However, it so became apparent that he really was in renal failure. We had then no explanation for the underlying renal disease.

Dr. John W. Littlefield: I should like to know if anybody knows what happens to the potassium in renal azotemia? Is that a differential point? Is there evidence of potassium intoxication just from dehydration?

Dr. Currens: I think some of the changes that have been reported in Addison's disease are probably of that nature in which the renal function is quite poor probably as a result of the electrolyte in balance of the serum. There may be retention of the potassium to the point that it tends to produce the electrocardiographic evidence of potassium intoxication. That is the only one that I can think of just now.

CLINICAL DIAGNOSIS

Uremia

Chronic glomerulonephritis, acute.

DR. SHORT'S DIAGNOSIS

Cortical necrosis of kidneys.

Periarteritis nodosa due to hypersensitivity to antibiotics.

ANATOMICAL DIAGNOSIS

Glomerulonephritis, acute.

Intracerebral hemorrhage, right.

PATHOLOGICAL DISCUSSION

Dr. Tracy B. Mallory: Autopsy showed two important findings. The first was the kidneys, which were very much enlarged, weighing 500 gm., and showed smooth, pale surfaces dotted with petechial hemorrhages – a gross picture that was quite characteristic of an acute glomerulonephritis. Microscopical sections confirmed that. Every glomerulus was involved, with both capillary obliteration and marked formation of epithelial crescents. There were just a few minute old scars of vascular lesions in the kidney, but I do not think that there had been any significant degree of chronic glomerulonephritis antedating this attack. The reason why the patient died so shortly after the period of dialysis was explained when the head was examined, revealing a very large cerebral hemorrhage, which Dr. Richardson can dscribe for us.

Dr. Edward P. Richardson Jr.: When the brain was examined, it was apparent from the flattening of the convolutions of the right hemisphere, and also by evidence of herniation of the medial aspect of the right temporal lobe through the opening of the tentorium, that there was a large mass within the right hemisphere. On section of the brain we found a very large cerebral hemorrhage within the right hemisphere. The blood within it was fresh, and it could not have been of any long duration. It assuredly was the cause of death in this case. In addition scattered thoughout the midbrain and pons were multiple hemorrhages. Hemorrhages of that type are seen in cases of increased intracranial pressure and frequently are associated with temporal herniation such as we found in this case. They were secondary to the large space-taking mass within the cerebral hemisphere, and they probably resulted in the very rapid demise.

Dr. Alfred E. Kranes: Would it be proper to ask Dr. Smith whether the heparin used here might have been responsible for this?

Dr. Smith: I think it might have been. We give large doses to all these patients. This represents a calculated risk in these severely ill patients, who may have hypertension and diffuse vascular disease. Although this represents the first serious complication of the procedure in our 12 patients to date, it illustrates that vividialysis is still more than elective procedure.

GENERAL PRACTICE STILL THE BIG FIELD IN MEDICINE

In spite of the rapid expansion of specialization, and the growing number of Boards to qualify specialists, general practice still dominates the field of medicine. General practitioners are still responsible for 75 per cent of the total pediatric care, 76 per cent of the obstetric and a great deal of the surgical care. Yet, I can recall a very heated discussion in a hospital council meeting over the privileges which general practitioners should have in the hospital work; whether they should be allowed to remove tonsils, deliver babies, give anesthetics or do any type of surgery. Collins and Clark (The New England Journ. of Med., Jan. 22, 1953) very ably discuss "General Practice, Today and Tomorrow." They discuss the problems of general practice in rural areas in contrast with those in urban areas, and the functions of the general practitioner in different circumstances. This article which is in two parts (second part published later), closes with attempt to define what is meant by "general practice." It would pay any doctor who looks upon himself as a general practitioner to take time out and read these articles. They will be found in the County Medical Library. W.W.W.

The PRESIDENT'S *Page*

THE SIXTY-SECOND ANNUAL MEETING HAS COME AND GONE, AND A NEW PRESIDENT FOR THE YEAR 1953-54 APPEARS ON THIS PAGE. HIS CHIEF MESSAGE THIS MONTH IN ONE OF THANKS TO THE MEMBERSHIP OF ARIZONA MEDICAL ASSOCIATION FOR HAVING ELECTED HIM TO THIS HIGH OFFICE, AND HIS CHIEF HOPE IS THAT HE MAY PROVE WORTHY OF YOUR CONFIDENCE.

AS A REPRESENTATIVE OF YOUR SCIENTIFIC ASSEMBLY COMMITTEE DURING THE PAST YEAR, THE COMMITTEE AND I WISH TO THANK YOU FOR THE MANY VALUABLE SUGGESTIONS WHICH WERE MADE, AND THE HELP WHICH YOU GAVE. IF YOU PROFITABLY ENJOYED THE SCIENTIFIC SESSIONS IN TUCSON THIS YEAR, REMEMBER THAT THE PROGRAM WAS MADE SUCCESSFUL THROUGH SUCH ASSISTANCE, AND THAT EACH SUCCESSOR WILL WELCOME ANY AID YOU CAN GIVE. IF YOU HAVE WITHHELD CONSTRUCTIVE CRITICISM FROM A SENSE OF BASHFULNESS IN YEARS PAST, SIT DOWN NOW AND WRITE YOUR RECOMMENDATIONS TO THE NEW PRESIDENT-ELECT OR TO ME.

EDWARD M. HAYDEN, M. D.
PRESIDENT ARIZONA MEDICAL ASSOCIATION

Editorial

ARIZONA MEDICINE

Journal of

ARIZONA MEDICAL ASSOCIATION, INC.

VOL. 10 MAY, 1953 NO. 5

CONTRIBUTORS

The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

EDITORIAL

STEP BACK BUD, I'M A FIRST AIDER

There is a well known story concerning the physician who was called upon to administer first aid to the victim of an automobile accident. He had no more than started his services when some burly individual elbowed his way through the crowd, rudely pushed the doctor aside, saying "Step back, Buddy, I'm a first aider, I'll take over." This is somewhat humorous in fiction but becomes considerably less so in fact.

A physician acquaintance of ours almost had just such an experience recently. He happened on the scene of an accident shortly after its occurrence and stopped to render whatever aid possible. He found an old man lying unconscious beside a partially wrecked car with his head lying in a pool of blood. His daughter was bending over him wringing her hands and vainly trying to recall him to concsiousness but doing nothing whatever about the bleeding. The physician hastily improvised a pressure bandage from the materials he had at hand, stopped the bleeding and brought the old man back to consciousness, examined him for other injuries and took charge generally of the medical situation much to the relief of the investigating officer who had meantime arrived. He stayed with the patient until the ambulance arrived. Upon its arrival about 25 minutes after the accident, he attempted to tell the ambulance driver and his assistant what had been done, the condition of the patient, information which he felt would be useful to them in the transportation of the patient to the hospital. He was completely ignored, the attendants rushed in to the patient, turned him over immediately on his back without investigating as to whether he had a back injury and unceremoniously ripped off the bandage which the physician had applied. At this point the investigating officer interrupted them saying the patient had been prepared by the physician for transport whereupon the physician received the comment with no note of apology that a different type of bandage was needed. Since the first aiders had obviously taken over, the physician immediately took his departure.

This incident is related in some detail since it illustrates an event which we hope does not occur often. It points up to the fact that is is highly desirable that a large number of people be trained in first aid but points up perhaps also that one aspect of this type of work may have been neglected. This physician was not shown courtesy which should have been due

any citizen who had done his best under the circumstances. Perhaps it was due to thoughtlessness and we, being charitable, prefer to believe so. However, it might not be amiss for first aid courses to include at least one lecture which might be entitled "Courtesy to Other First Aiders, Even if They are Doctors."

Believing that the following article would be of interest to the Physicians of Arizona many of whom knew and loved Dr. Coleman we have asked for and received permission from its author Bert Fireman for its republication. It appeared originally in Mr. Fireman's column UNDER THE SUN in the Phoenix Gazette, February 10, 1953.

Editor

UNDER THE SUN

From the lounge of the Kiva Club we could look out over the Valley of the Sūn and across the indefinite dusty course of the Salt River to the Sierra Estrella mountains looming in the southwest and the Santans to the southeast. Lunch was over; my usual hearty noonday meal topped with three or four cups of coffee, but the doctor had sprinkled his smoked tongue and tomatoes heavily with salt and then only toyed with the food. He was more interested in talking about that part of Arizona beyond the Gila River, so when I had finished we moved around to soft seats overlooking Southern Arizona.

Since he first came to Arizona a few winters before, Dr. Claude C. Coleman of Richmond, Va., had been tremendously interested in the strip of Arizona south of the Gila. In history it is known as Gadsden Purchase. Just 100 years ago, seeking a low-level railroad route to the Pacific, the United States government invested $10 million in the parched strip of ground stretching from the Rio Grande to the Colorado. James Gadsden, amabassador to Mexico and railroad speculator, was accused of extravagence in the transaction. He has been vindicated a hundred times. Last year, for example, Arizona counties located within the Gadsden Purchase produced $76 million in minerals alone.

Dr. Coleman was a healthseeker, and winter visitor. In his suite in the Westward Ho he kept oxygen flasks for relief when asthma attacks came on. His regular breathing was labored. He could only walk short distances. A nurse-secretary and Mrs. Coleman were always near to attend him.

Despite the asthma that made him an invalid, Dr. Coleman was studying the early history of Arizona as vigorously as his health permitted. His particular interest was in the doctors, both military and civilian, who had ministered to the sick and injured of the region before statehood.

Somewhere in the past Dr. Coleman had stumbled onto the fact that at least three great military doctors—Leonard Wood, Walter Reed, and J. B. D. Irwin—had practiced in Arizona early in their notable careers. Before Dr. Walter Reed discovered the cause and manner of transmission of yellow fever, he was highly regarded as a private practitioner in Arizona. Both Doctors Wood and Irwin won the Congressional Medal of Honor for heroism during the Indian wars in Arizona. General Wood also had been a cattle rancher in Arizona. He was a leader of the Rough Riders in the Spanish American War and a capable military administrator of occupation forces in both Cuba and the Philippines following that war. After leaving Arizona, Dr. Irwin established the first tent field hospital on a battlefield. That was at the battle of Shiloh in Tennessee during the Civil War. His innovation greatly reduced deaths from battle wounds.

UNFINISHED WORK: Dr. Coleman and I had lunch together several times during the last two winters, sometimes at the Kiva Club and once or twice in his suite when he wasn't feeling well. Last winter's cold and wet weather didn't help his poor health, but he optimistically had expected to return this season for more sunshine and warmth. Two weeks ago his secretary wrote me that Dr. Coleman had died on Jan. 9, at the age of 73.

The death of the former neurosurgeon and professor of neurosurgery left his *planned book on the doctors of Gadsden Purchase* unfinished. *But in the December issue of the Virginia Medical Monthly there was published a paper he had written as a preliminary outline of the projected book.*

In it he had traced the history of the Gadsden Purchase and touched on the careers of outstanding territorial doctors. After telling about Doctors Reed, Wood and Irwin, he went into detail on the exploits of Dr. George E. Goodfellow, the famous gunshot specialist of Tombstone's turbulent days. He probably had the greatest experience in gunshot wounds of the intestines of anyone in America, Dr. Coleman wrote, "but he lamented the fact that he could never cure a case

of gunshot perforation of the intestine." Dr. Goodfellow's greatest fame came as a pioneer in prostatectomy. He has been credited with being the first surgeon to completely remove the prostrate gland through a perineal incision. He reported 78 out of 80 such operations with complete success, "A most creditable record for any era. It was said he operated on many of his patients in the early days on a door laid across two whiskey barrels." Dr. Goodfellow later became chief surgeon for the Southern Pacific Railroad in Arizona and then Sonora.

Dr. Coleman noted the great strides in medicine in Arizona, where "not so long ago the doctor had to be as adept with a six-shooter as he was with the scalpel. Today they have many well-equipped hospitals and many prominent doctors, whose voices are heard in the councils of the national medical profession."

Among the famous "medicine men" of Arizona Dr. Coleman even listed Geronimo, the surly, vicious last leader of the renegade Chiriachua Apaches. Geronimo was no chief—but a medicine man who devoted most of his time to making bad medicine for the whites.

We'll miss those pleasant winter visits with the distinguished Virginian who was fascinated with the history made in Arizona by members of his profession.

BOOK REVIEWS

THE LITERATURE ON STREPTOMYCIN
By Selman A. Waksman, Rutgers University Press, New Brunswick, New Jersey, December 19, 1952. Price $5.00.

The handsomely bound volume contains 5,550 bibliographic references on streptomycin and the enumeration of these references occupies 440 pages of the book. The author index occupies 61 more pages and the subject index 44. This provides a total of 553 pages of reference material on streptomycin put up in a handsome blue binding with silver lettering. It seems that this would be very useful for reference libraries, especially in institutions where there is need for information on streptomycin for use in treatment or research. The ordinary practicing physician will probably not want to add it to his library but probably would be very glad to have it available in his medical association or hospital library.

LIVING WITH CANCER
By Edna Kaehele, Doubleday and Company, Inc., Garden City, N. Y., 1952. Price $2.00.

This book is a fascinating account, chronologically arranged, of experiences of a woman who almost died of cancer but didn't. Anyone who has come face to face with the stark realization of possible death will recognize here many of his own thoughts which have been put into print. It is interesting to note that this patient began to improve when she conquered her fear of death although it is a little hard to tell which came first.

There is one disappointment in the book; and that is that I believe the author has been unfair with her physicians and especially the radiologist. Althought she, in so many words, gives him a certain amount of credit for her recovery, one feels that this is done rather grudgingly and that in her heart she feels that she has been over treated or ill treated and has survived in spite of her doctors rather than because of them. As a matter of fact, speaking as a radiologist, it is my feeling that from her description of the treatment which she has had that her radiologist was rather heroic in giving her the heavy treatment which he did and if he had not done so it is doubtful if she would have survived.

There is no doubt that this is a book which will provide a great deal of encouragement to cancer sufferers. I feel that it should not be used indiscriminately, however, but should be judiciously prescribed. I, therefore, recommend that the physician read the book himself before recommending it to his patients. It is a small book and can be read in one evening.

TOPICS OF *Current Medical* INTEREST

RX., DX., AND DRS.

By GUILLERMO OSLER, M. D.

We should start one paragraph each month with the heading "ALVAREZ SEZ,—" since we quote him almost that often. . . . This month, in his small journal 'Modern Medicine', he editorializes on ROENTGEN THERAPY AND CANCER OF THE BREAST. His old friend at the Mayo Clinic, Dr. Stuart 'Tack' Harrington, has surveyed their results over a 30 year period. . . . If all cases are considered, the radiated ones did 8% better. If only those with no metastases in the axilla are considered, the ones NOT radiated did better. If there were axillary metastases, the radiated cases did slightly better. . . . The results are not encouraging.

The pendulum swings back, and in doing so it may knock a lot of people (and companies) down, perhaps. . . . 'Perhaps' is the word, since we are no more sure that the ANTI-CHLOROPHYL REPORTS are true than we are that the favorable reports (and advertising) were solid and reliable. . . . If it turns out that the destructive, scornful new opinions are factual, it will be one of the greatest sells (in more ways than one) of drug history. . . . It would seem wise to wait; then, if it still seems wise, look up the names of the people who first boomed chlorophyl as a deodorant and put them on a list.

Most of us know what we know about certain ANTIBIOTICS from drughouse literature, and it's a fairly good source too. . . . Some news comes, later, from medical journals. If the physicians who write for these use generic terms for the drugs, most of us would be frozen stiff. . . . Who would know that carbomycin could mean 'Magnamycin'? Most could guess that chloramphenical is "Chloromycetin', and that erythromycin is possibly "Ilomycin' or 'Erythrocin'. You'd have to scratch your head on oxytetracycline (of which Terramycin is a brand). . . . It might be easier to simply use the brand names, since most of the companies discovered the drugs.

Carroll Palmer, director of the T.B. Research Office, W.H.O. in Copenhagen, has shown that considerably diluting BCG VACCINE has little effect on the size or duration of the resultant tuberculin skin test. . . . Also, room temperature instead of refrigeration does not produce serious differences. . . . Further, the varying number of 'takes' in different areas of the world (often from single batches of vaccine) may be due to the effect of sunlight on the ampules. . . . This latter effect may not apply to vaccine made by the Research Foundation in Chicago, since they now use the lyophilized (dried) preparation instead of the liquid suspension.

Arizona has been remotely connected with AN ARTICLE IN THE JAMA, even tho it is 'post hoc, ergo propter hoc'. . . . Dr. U. V. Portmann of Tucson was former head of a department at the Cleveland Clinic, and wrote a paper with E. P. McCullagh on 'Developmental Defects Following Irradiation of the Ovaries in a Child'. . . . If he has other papers stacked away, I bet I know where he could have them published.

FLUORIDATED WATER has become not only scientifically approved but 'the mode'. How does one know? Easy — the bottled water companies are advertising it and supplying it.

The use of radioactive gold in treatment of CANCER OF THE PROSTATE is a novel method, not very well known. H. Dabney Kerr and colleagues of Iowa City report good early results, better than with other methods. . . . The part of the report which is most surprising and shocking is that which tells of the incidence of prostatic Ca. I'd never guess it, and maybe you wouldn't. Twenty per cent of men over 40, or a total of 3,000,000 men in the United States have prostatic Ca., so they say.

CALCIFICATION may occur in non-malignant lesions of the lungs, and is a differential point between them and cancerous tumors. . . . This difference is hard to see on regular chest films, but Good, Hood, and McDonald of Rochester, Minn., have shown that body-section radiography brings it out clearly. . . . If the lesion has no visible calcium, it is a point in favor of exploration.

Neostigmine has been shown to CONTROL SEX HORMONES in rats. It is hoped that the results may be transposed to humans, where the drug has numerous uses. Maybe it will have some effects on the growth of neoplasms. . . . It is interesting to speculate on how the new data fit in with the known effect which neostigmin (called prostigmin, or even physostigmine) has in starting a reluctant menstrual period.

In case you favor the use of the GOFMAN LIPROPROTEIN TEST, you might recognize at once the name of the place where they do them. . . . In case you think the tests are not definitive, or are too expensive, or in case you are indiffer-

ent about them, the name 'Cardiovascular Laboratory Section, The Institute of Medical Physics' would cause a raised eyebrow. . . . Who can be a medical snob, however, if the test turns out big?

Using a "LIE DETECTOR" instrument does not mean that one is a psychologist or a detective; one may be a dermatologist. . . . Finding the cause of a skin disease may require the talent of a Hawkshaw, but only recently Drs. Perry and Mount have applied one of the emotion-testing devices to a study of sweat glands and skin health. . . . An increase in electrical resistance results from an increased activity of the glands. It could give leads to diagnosis, and also to the use of drugs.

A columnist must be allowed an 'I told you so' every now and then, altho it probably should be limited to once a month, or some such ration. . . . About three years ago an odd report was noted in the Michigan State Medical Journal about a Detroit surgeon who SANDPAPERED ACNE with great success, and it was reported here. . . . The current Sat. Eve. Post tells the origin of the method which was started between 1942 and 1945 by a Dr. Preston Iverson of Philadelphia. He started using it on tattoo marks, then war 'tattoo' marks on the face, and then on various other superficial blemishes. . . . About two-thirds of the skin thickness is removed, and the glands and hair follicles remain.

The use of vitamin A to improve NIGHT VISION, or to correct a deficiency in dark adaptation, is of more than a dozen years duration. Dr. Jeans even had a measuring device by that time. . . . The newest angle is that such methylating agents as methionine and vitamin B 12 are an aid to utilization of vitamin A. . . . Oral administration of methionine has already been shown to improve dark adaptation, and probably by the means mentioned. The improvement begins in an hour and lasts 24 to 32 hours.

Graphs and pie-shaped devices are of great help in showing changes in statistics which would not be impressive by themselves. . . . We were surprised enough by some charts in 'Hospital Topics' to look again, and write this down. . . . The first was a graph with a black column for each year's average census in hospitals from 1934 to 1952. The steps rose from 830,000 to 1,293,000, with an irregular higher peak during the war. (It looked like a huge rise because the baseline was not zero, but 800,000). . . . The pie for 1952 had only three unequal pieces,—The smallest slice was the 3% of patients who were cared for in proprietory hospitals; the second largest slice was the 22% who were in non-profit hospitals; the huge part of the pie, in black, was the 75% who were in government hospitals. 'Pie figures' are astounding.

This month's MOST INTERESTING WORD applies to a product from our favorite laboratory, Abbott's. They won't like it if someone makes fun of it, but they chose the name 'Fumidil', and if it sounds like an epithet from Amos and Andy they have no one else to blame. . . . It doesn't sound like 'a new direct-acting amebicile antibiotic', but it is. . . . Again, say we, the names of drugs should sound like what they are—or at least not like something else (or certainly not like something funny). . . . Maybe they follow the course set by a public figure of the 1920's, who urged people to say anything they pleased about him as long as his name was spelled right.

NOTICE

ALL CONTRIBUTORS OF ARIZONA MEDICINE SHOULD HAVE THEIR MATERIAL IN THE JOURNAL OFFICE NOT LATER THAN THE 15th OF THE MONTH PRIOR TO PUBLICATION IN ORDER TO HAVE ARIZONA MEDICINE REACH ITS READERS ON OR BEFORE THE 15th OF THE MONTH.

Material arriving after that date will be published the following month.

Symposium On Heart Disease

The Twenty-Fourth Annual Postgraduate Symposium on heart disease will be held at the St. Francis Hotel October 28, 29, 30, 1953.

The San Francisco Heart Association, which has presented this annual postgraduate series for twenty three years has this year invited five Northern California Heart Associations to participate in bringing to San Francisco a large contingent of distinguished guest speakers for the occasion. Sharing the planning with the San Francisco Heart Association will be the Heart Associations of Alameda County, Contra Costa County, Monterey County, San Mateo County and Santa Clara County.

Four guest speakers have already accepted the invitation to participate. They are Doctors Herrman Blumgart of Boston, Howard Burchell of Rochester, Minnesota, Robert L. King of Seattle, and Paul Wood, Dean of the Institute of Cardiology, London, England.

The Arizona Medical Association, Inc.
LEGISLATIVE COMMITTEE
1952-53 ANNUAL REPORT

It is with pleasure that the Legislation Committee of this Association submits its annual report relating to its activities before the Twenty-First Legislature of the State of Arizona, first regular session. It should be pointed out that following deliberation of Council, due to the many complexities involved in the activation of a new legislature, it was determined expedient not to sponsor nor support too many bills during its first regular session. Also it was realized that during its first session following numerous referendums adopted by the people in the general election many bills would be introduced requiring deligerate consideration and consuming appreciable time of this body.

CORONER'S INQUEST AND VITAL STATISTICS

H.B. 141 relating to coroner's inquest, amending Section 44-3405, Arizona Code of 1939, sponsored by your Association, enacted into law by the Twenty-First Legislature of the State of Arizona, first regular session, signed by the Governor, March 28, 1953, becoming Chapter 78, provides that the coroner may issue subpoenas for witnesses, returnable forthwith, or at such time and place as he may appoint, which may be served by any competent person. He must summon and examine as witnesses every person who, in his opinion, or that of the jury, has any knowledge of the facts, and he shall summon a qualified physician to examine the body and, if necessary, conduct an autopsy, and give an opinion as to the medical cause of death unless such medical examination has already been performed and such opinion has already been rendered. All statements shall be signed by a qualified physician. A witness served with a subpoena may be compelled to attend and testify, or be punished by a justice of the peace. Provided, however, that anything in this Act to the contrary notwithstanding, the securing of a medical examination, autopsy, and certification as to the medical cause of death hereinabove provided, unless directed by the jury, shall be discretionary with the coroner if no qualified physician be readily available at the place where the inquest is held.

H.B. 142 relating to vital statistics, amending Section 68-606, Arizona Code of 1939, and amending Chapter 68, Article 6, Arizona Code of 1939, by adding Section 68-606a, likewise sponsored by your Association, enacted into law by the Twenty-first Legislature of the State of Arizona, first regular session, signed by the Governor, March 28, 1953, becoming Chapter 79, in conection with "referral to coroners," provides:

(a) Any person having knowledge of the death of a human being, which, for the purposes of this Act shall include a fetal death, in a case in which no physician was in attendance at the time of death, shall forthwith report to the nearest peace officer all information in his possession regarding the death and the circumstances surrounding it. The peace officer receiving such report shall immediately make or cause to be made an investigation of the facts and circumstances surrounding the death and report the results thereof to the coroner.

(2) The local registrar shall forthwith refer the following cases and all information he has regarding the same to the coroner: 1. when no physician was in attendance during the last illness of the deceased; 2. when a physician in attendance is physicially unable to supply the data, or, 3. when circumstances suggest that death was caused by other than natural causes.

(c) Hospitals shall forthwith report to the coroner all information they have regarding hospital deaths where there is no attending physician.

(d) When circumstances suggest to the physician in attendance that the death was caused by other than natural causes, he shall refuse to sign the death certificate and forthwith report all information he has regarding the same to the coroner.

As relates to "Investigation as to the cause of death and signing of death certificate" the law now provides:

(a) The coroner shall immediately make or cause to be made an investigation of the facts and circumstances surrounding the death to determine if the death was natural, accidental, suicidal or homicidal, and its medical cause. He shall direct the medical examiner or any other qualified physician to make such examination of the body as may seem necessary including, if needed, an autopsy to determine the medical cause of death. Such medical examiner or other qualified physician shall promptly report his findings to the coroner and sign the death certificate certifying as to the medical cause of death together with giving such other infor-

mation as may be required by the state registrar. If the coroner be a physician he may personally make such medical examination and sign the death certificate as to the medical cause of death. After receipt of information as to the medical cause of death and after investigation concerning the facts and circumstances surrounding the death, the coroner shall also sign the death certificate stating whether the death was natural or accidental, or, if the information gained by the coroner as the result of these investigations is such as to cause him to suspect that the death was suicidal, homicidal or occurred suddenly under such circumstances as to afford a reasonable ground to suspect that the death was occasioned by the act of another by criminal means, he shall so certify on the death certificate together with giving such other information as may be required by the state registrar. The county attorney shall be apprised by the evidence gained and the conclusions reached as the result of such investigations and the complete file thereon shall be made available to the county attorney.

(b) Where an autopsy has been performed pursuant to this Act, no cause of action shall lie against any coroner, physician or other person for requesting or participating in such autopsy.

(c) The board of supervisors, upon request of the county attorney or coroner, may appoint and fix the compensation of a regular medical examiner for performing the medical examinations and certificates required by this Act. The person appointed must be a qualified and practicing physician. In the event no regular medical examiner is appointed and the coroner is not himself a qualified physician, the board of supervisors shall provide for appropriate compensation for the qualified physician employed to conduct the medical examinations, certifications, and, if needed, the autopsies required to be performed by this Act.

(d) Phovided, however, that anything in this Act to the contrary notwithstanding, the securing of a medical examination, autopsy, and certification as to the medical cause of death hereinabove provided shall be discretionary with the coroner if no qualified physician be readily available either at the general locale of the death or the proposed place of burial or the locale of the mortuary if the body is to be sent to a mortuary in preparation for burial.

For many years there have been complaints by private citizens, members of the medical profession, the State Board of Medical Examiners, State Department of Health and Vital Statistics concerning so-called "mystery deaths" occurring the the various counties, which are those deaths that should be carefully investigated to determine their cause, but for some reason or another were not so investigated. Complaints regarding these activities fall usually into two categories. The first is that of law and order. Private citizens and others believe that due to laxity in the statutes concerned, many crimes have actually been ignored and passed off as death by "natural cause" when, as a matter of fact, there may have been a suicide or homicide involved which would have been revealed by a medical examination. Second, medical men in our state are anxious that our Department of Vital Statistics more accurately reflect the true medical cause of death in order that the information gained by the study each physician gives to these vital statistics as to health trends and tendencies in our state be accurate.

Presently at a coroner's inquest a physician *may* be called upon and may be asked to certify as to the cause of death. Chapter 78 *requires* that a qualified physician shall be summoned to examine the body, and, if necessary, conduct an autopsy, and give an opinion as to the medical cause of death unless such medical examination has already been performed and such opinion has already been rendered. All statements shall be signed by a qualified physician. This will insure first, that a doctor aid the coroner and the coroner's jury in discovering whether the death is natural or accidental, or on the other hand suicidal or homicidal, by giving the coroner and his jury the benefit of medical knowledge as to the true medical cause of death. Second, it eliminates having the doctor make a decision as to whether the death was suicidal, homicidal or natural, a job for which law officrs are trained and doctors are not, usually.

Further the law presently provides for reporting to the coroner by private individuals and the local registrars a death that seems suspicious. Chapter 79 adds to these two groups the requirement of reporting to the coroner hospital deaths where there is no attending physician (if there be one), seems to be from other than natural causes. The purpose of these additions is to in-

clude those emergencies brought into a hospital where the hospital has no knowledge of the patient or the cause of his death and also to include deaths where th attending physician suspects foul play.

Presently the law permits that once a death is reported to the coroner, he must make an examination to determine the cause of death and may employ a physician so to do. Chapter 79 requires the coroner to employ a doctor to make this examination including, if necessary, an autopsy, and certify as to the medical cause of death. After the medical examination the coroner is then in a better position to determine the true cause of death. The now existing law also gives protection and immunity to the coroner, the doctor and all others who may be concerned in requesting an autopsy if the same is necessary and in performing it.

COMPACT FOR WESTERN REGIONAL COOPERATION IN HIGHER EDUCATION

Most of you will recall that your Association last year supported legislation which was enacted into law (Chapter 104, March 25, 1953), for ratification and approval of the Compact for Western Regional Cooperation for Higher Education with the states of California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming and the Territories of Alaska and Hawaii. Through this action it is believed that the western states, or groups of such states within the region, who individually do not have sufficient members of potential students to warrent the establishment and maintenance within their borders of adequate facilities in all of the essential fields of technical, professional and graduate training, nor do all of the states have the financial ability to furnish within their borders institutions capable of providing acceptable standards of training in all the fields mentioned, cooperatively can provide acceptable and efficient educational facilities to meet the needs of the region and of the students.

Subsequently the Governor appointed a commission comprising three resident members of this state, namely: Dr. O. H. Wedel, 3828 Calle Cortez, Tucson; D. W. Melick, M.D., 15 East Monroe, Phoenix; and Mr. Alexander A. Raisin, P.O. Box 2164, Phoenix, to administer the duties prescribed. As a result of their deliberations that body introduced S.B. 115, passed by the Twenty-First Legislature, first regular session, signed by the Governor, March 25, 1953, becoming Chapter 59. This measure had the support of your Association and provides for the operation and administration of the compact, the processing and certification of qualifying students by the Board of Regents of the university and State Colleges of Arizona, requiring contract with students certified and designating terms, conditions and collection thereof, and providing for an appropriation to be expended during the forty-first and forty-second fiscal years for expenses of the Arizona members of the commission ($4,800); contribution by the State of Arizona, to the general expenses of the commission ($7,000); tuition for medical students ($37,500) tuition for dental students ($9,600); and tuition for veterinary students ($6,000).

The board shall, within the limitations and on the terms as fixed by the commission and by this Act, determine the number of students desiring to take advantage of the educational facilities afforded by the compact; and from those indicating a desire to participate, select a group in each allowable professional field equal to three times the number possible for participation in a given school year. In making such selections the board shall only include such students as: (1) who have at least average scholastic attainment record; (2) who are citizens of the United States; (3) who have been actual bona fide residents of the State of Arizona for at least the last ten (10) years, and, (4) who have completed such preliminary education as will qualify them for admission to the professional or graduate school provided by the commission.

The names of those students, selected as aforesaid, shall be certified by the board, via the Arizona members of the commission to the commission, along with such data as the commission may require.

Before certifying a student to the commission, as herein provided, the board shall enter into a written contract on behalf of the State of Arizona with such student, said contract to cover the methods and terms of repayment by said student to the State of Arizona, said contract to be on such terms and conditions and in such form as provided by the board, except that said contract must provide:

(1) That said student shall within one (1) year after completing his professional education and internship, begin the practice of his profession within the State of Arizona, except if said stu-

dent engage in postgraduate studies and do so without a lapse of more than one year following the completion of his professional course, then said practice shall be commenced within one (1) year after the completion of said graduate studies:

(2) That if said student engages in the practice of his profession within the State of Arizona, as herein provided, his indebtedness to the State of Arizona may be discharged as follows: (a) by the payment to the State of Arizona of all sums expended by the State for and in behalf of such student, or (b) for each two (2) years of practice there shall be discharged his obligation for each one (1) year of study for which a portion of the cost thereon was paid by the State of Arizona;

(3) That if said student fails to complete the required course of professional study, or if said course of study is interrupted by one school year or more for a cause or causes other than for a total disabling illness or injury, or if said student fails to practice his profession within the State of Arizona for such continuous time as to completely discharge his obligation, the entire sum paid for or on behalf of said student by the State of Arizona and not repaid or discharged as herein provided, shall be due and payable forthwith, together with interest at the rate of four per cent (4%) per annum from the date or dates of disbursement by the State of Arizona.

LEGISLATION OF INTEREST TO MEDICINE

There were, of course, other bills introduced sponsored by various groups or individuals the contents of which were of interest to medicine; (a) the testing of dairy cattle for brucellosis (b) creating the Department of Public Health and Welfare (c) temporary disability benefit insurance for protection against loss of earnings due to sickness and accidents (d) appropriating funds for the construction of an addition to the State Tuberculosis Facility at Tempe (e) providing for minimum standards relating to the operation of the State Department of Public Health (f) provision for the vivisection of animals (g) providing for a depository for blood, bones, eyes and cartilage (h) providing for improved standards in the licensing of chiropractors (i) appropriating additional funds in connection with purchase of site, construction and equipment of a State laboratory (j) defining narcotic drugs (k) creation of the office of State Medical Examiner and (l) providing for the regulation of the practice of optometry. Council was not requested nor did it take any official action on these measures. Certain objections were raised to the optemetry bill and through consultation a satisfactory amendment thereto was realized. Regarding the bill creating an eye and bone bank, this measure was introduced near the close of the session and while of special interest to the doctors, it was considered wise to withhold support until certain legal entanglements can be wisely and adequately removed. On the recommendation of Council study will continue through the coming months and it is the hope that a proper bill may be readied for introduction during the second regular session of the legislature. The bill pertaining to vivisection was introduced by a new legislator hailing from Pima County, and was not considered adequate. You will recall that the Association sponsored similar legislation a few years ago which passed the House but died in committee of the Senate. At such time as the need for vivisection has been adequately established the committee will give further serious consideration to another attempt to have enacted into law such worthwhile legislation. It is of interest to note that the bill relating to temporary disability benefit insurance was not introduced by the Employment Security Commission of Arizona, which body following previous hearing attended among others by the members of the medical profession, had determined on the basis of its findings that the need therefor had not been sufficiently established to warrant further consideration at this time.

Two bills were introduced and passed relating to workmen's compensation; one providing for a more equitable adjudication of claims and the other setting aside one per cent of premiums collected for rehabilitation. Following conferences planned to be called during the coming months, further amendments to the act will be proposed in line with need as previously expressed and contained in report of the Industrial Relations Committee of this Association, submitted last year.

"COMMENDATION"

It is again gratifying to observe that those bills actually sponsored by your Association successfully cleared the legislature and became law on signature of the Governor. Much credit is due and given to our Association Attorney, Mr. Ed-

ward Jacobson, whose able advice and astute leadership has immeasurably raised within legislative circles the prestige of the medical profession of this state during the past several years. Your Legislation Committee is humbly proud and wishes to express its grateful appreciation to the Governor, members of the Twenty-First legislature and others of our Association who have lobored arduously during the past several months in the interest and support of sound health legislation.

Respectfully submitted,
Jesse D. Hamer, M.D.
Chairman
Legislation Committee

MALPRACTICE INSURANCE SURVEY

During the past several weeks your Central Office has been deluged with inquiries regarding professional liability (malpractice) insurance rates in Arizona. It set out to obtain factual information from qualified experts in the field and this informative report is prepared in the hope that it might contain answers to some of the questions in the minds of many of our medical doctors.

As you are all aware, an increase in (malpractice) rates in Arizona was effected in the fall of 1952. It should be borne in mind that prior to this time the base rate in this state for such coverage with $5,000/15,000 limits, one-year term, was $25, which was constant and remained unchanged from 1931 until 1952—a very favorable situation in the light of a very unfavorable experience nationally in the steadily increasing number of suits filed against doctors alleging malpractice. The base rate was increased from $25 to $35 with a 50% surcharge added for major surgery. In addition there is a 50% surcharge for partnership coverage for such physicians desiring to be covered not only for their individual practice but also for their partnership liability, which under such conditions, of course, is recommended.

I believe it is recognized among our doctors that the Arizona experience has been somewhat better than that in our neighboring state of California, and our rates indicate this. For example, where our base rate is now $35 for $5,000/15,000 limits, the base rate in California is $100, San Francisco and Alameda County; $90 in Los Angeles County and $75 in the remainder of the state. New Mexico has a base rate of $50 and Utah a base rate of $45. Additional states whose recorded rates are in excess of the current Arizona base rate are:

Colorado	$50	Ohio	$40
District of Columbia	65	Oklahoma	50
Florida	45	Oregon	45
Indiana	60	South Dakota	60
Minnesota	60	Tennessee	40
Montana	50	Washington	60
Nevada	50	Wisconsin	50
New York	Below	Wyoming	50

NEW YORK: Reports basic premiums $5,000/15,000 limits) increased 100% since 1947. Present rate, Non-surgery, $86; X-ray Therapy (superficial), $96; Deep and Superficial, $106; Electric-shock, $126; Surgical only, $116; plus X-ray Therapy $126 to $136; plus Electro-shock $156; and Cosmetic Plastic Surgery, $146.

It is observed there is a constant tendency toward more suits and higher claims. Inflation has found its way into the trial courts as well as every where else and expenses continue to mount all along the line. In view of all of these factors it would appear that the new rates, while somewhat higher than those previously charged, may be considered reasonable.

Let us look at some Arizona statistics. The St. Paul Mercury Indemnity Company for the first nine months of 1952, reports physician-surgeon premium receipts of $9,517 against losses of $6,923. United States Fidelity and Guaranty Company, writing considerable malpractice coverage in this state, shows a record of all classes of malpractice insurance, which includes physicians, surgeons and dentists as follows.

Year	Premium Receipts	Losses
1949	$10,099.75	$14,099.25
1950	10,090.09	7,848.39
1951	10,508.72	24,670.56
1952	14,395.97	84,401.26

NOTE: It is pointed out that the 1952 loss experience reflects reserves for cases in various stages of litigation, principally one involving dentists; however, the general outlook for this year (1952) is anything but favorable.

These figures are recited to help you better understand the problems faced by all such insurance carriers and may very well be one of the reasons why the American Casualty Company withdrew recently from writing business in Arizona. You may recall that The Medical Protective Association withdrew from Arizona several years ago and has not seen fit to return to date. I think this particular phase of our survey will convince most of us that the malpractice business is not particularly a profitable one—even in Arizona.

The malpractice insurance market is an uncertain one with only a few companies actually writing such coverage in the state. The leaders are: St. Paul Mercury Indemnity Company; United States Fidelity and Guaranty Company; General Accident; American Employers and Lloyds of London.

Frequently our Council has been asked to consider the procurement of a group malpractice policy sponsored by the Association. It hasn't been recommended on good authority to date. In the first place it is questionable whether such group coverage could be procured from a reputable company at any real saving to the doctors, and second, on the basis of present day experience it must be held in mind that should such coverage be procured and the loss experience prove adverse, it is always possible the carrier might withdraw and at such time it might be impossible to interest other companies to write in Arizona.

A survey completed in November of 1952, among the state medical associations participating, disclosed nineteen had in effect sponsored professional group liability insurance and fifteen had not. Of the former group three had received notice of intention of the carrier to cancel the master policy certificates. The number of physicians covered per individual group contract ranged from a low of 150 to a high in excess of 14,000. From comments noted there would appear to be a national trend among major malpractice insurance carriers to withdraw from the field of group coverage. Most every state reported an increase during the past five years in the number of malpractice suits filed.

Regarding partnership liability, a legal opinion recites that the criterion of a partnership is whether its members share in the profits and losses. If they do, then a real partnership exists, and each physician who is a member of the partnership should pay a 50% surcharge to include his partnership liability under his personal malpractice policy. This does not apply to physicians who only share office expense, keeping their own practice and income separate.

Many physicians have asked for a comparison of base rates over and above the minimum basic limits, so to accomodate this wish the following table has been developed.

Limits	Physician		Surgeon	
	1 Year	3 Years	1 Year	3 Years
$ 5,000/ 15,000	$35.00	$ 87.50	$ 52.50	$131.25
10,000/ 30,000	47.25	118.13	70.88	177.20
25,000/ 75,000	59.85	149.63	89.78	224.45
50,000/150,000	66.15	165.38	99.23	248.08
100,000/300,000	72.10	180.25	108.15	270.38

NOTE: These rates are for individual physicians or surgeons not performing X-ray or Radium Therapy. If partnerships are involved, and as stated before, they are subject to a surcharge of 50%. In Arizona, today only one company is known to write a three-year term policy at 2½ times the annual rate and that is St. Paul Mercury Indemnity Company.

Special recognition is given with grateful appreciation to Edward H. Bringhurst, President, Standard Insurance Agency, Phoenix; Conner Johnson of the Conner Johnson Co., Phoenix, and Blaine D. Shimmel, Attorney, Phoenix, representing a number of professional liability insurance carriers operating in this state, who collaborated in the preparation of this report, together with the Medical Society of the District of Columbia, supplying a portion of the statistics recited.

The Arizona Medical Association, Inc.
Robert Carpenter,
Executive Secretary

Arizona Pharmaceutical Page

Resolutions Nos. 2 and 4

WHEREAS

THE OFFICERS AND COMMITTEES OF THE AMERICAN MEDICAL ASSOCIATION HAVE BEEN OF GREAT ASSISTANCE TO THE MEMBERS OF OUR ASSOCIATION DURING THE PAST YEAR AND HAVE EXTENDED OUR COMMITTEES MANY COURTESIES IN ATTENDING OUR COMMITTEE MEETINGS AND INVITING US TO PARTICIPATE WITH THEM IN THE DELIBERATIONS OF SOME OF THEIR PROBLEMS AND

WHEREAS

THIS SAME COOPERATION HAS BEEN EXTENDED TO THE MEMBERS OF OUR COUNTY ASSOCIATIONS BY THE OFFICERS AND MEMBERS OF THE MARICOPA AND PIMA COUNTY MEDICAL SOCIETIES

NOW THEREFORE BE IT RESOLVED

THAT THE ARIZONA PHARMACEUTICAL ASSOCIATION EXTEND ITS THANKS TO THE MEMBERSHIP OF THE ARIZONA MEDICAL ASSOCIATION, THE MARICOPA COUNTY MEDICAL SOCIETY AND THE PIMA COUNTY MEDICAL SOCIETY FOR THE COURTESIES EXTENDED AND PLEDGE TO THEM THE CONTINUED COOPERATION OF OUR ASSOCIATION IN ALL ENDEAVORS HAVING FOR THE MUTUAL BENEFIT OF OUR ASSOCIATION MEMBERS AND THE PATIENTS WITH WHOM THEY ARE IN CONTACT AND

BE IT FURTHER RESOLVED

THAT OUR ASSOCIATION EXTEND TO THOMAS H. BATE, M.D., PRESIDENT OF THE ARIZONA MEDICAL ASSOCIATION THEIR SPECIAL THANKS FOR THE SEVERAL OCCASIONS HE HAS MET WITH US AND FOR THE SPLENDID MESSAGE HE BROUGHT TO US AT OUR PRESENT MEETING.

WHEREAS

THROUGH THE COURTESIES OF R. LEE FOSTER, M.D., EDITOR-IN-CHIEF OF ARIZONA MEDICINE JOURNAL, THE OFFICIAL PUBLICATION OF THE ARIZONA MEDICAL ASSOCIATION, AND MR. J. N. McMEEKIN, PUBLISHER OF SAID JOURNAL, THE PUBLISHING COMMITTEE OF THE ARIZONA MEDICAL ASSOCIATION MADE AVAILABLE TO THE ARIZONA PHARMACEUTICAL ASSOCIATION A PAGE EACH MONTH IN THEIR PUBLICATION AND

WHEREAS

THE OPPORTUNITY OF DISSEMINATING THE VIEWS OF ARIZONA PHARMACISTS THROUGH THIS MEDIUM, TO THE PHYSICIANS OF OUR STATE HAS BEEN OF GREAT VALUE TO OUR PROFESSION.

NOW THEREFORE BE IT RESOLVED

THAT THE ARIZONA PHARMACEUTICAL ASSOCIATION EXPRESS ITS THANKS TO DR. FOSTER, MR. McMEEKIN AND THE MEMBERS OF THE PUBLISHING COMMITTEE OF ARIZONA MEDICINE FOR THE OPPORTUNITY AND FAVOR AND EXTEND TO THEM AND TO THE MEMBERS OF THE ARIZONA MEDICAL ASSOCIATION THE USE OF THE PAGES OF OUR OWN PUBLICATION, THE ARIZONA PHARMACIST WHENEVER THEY MAY DESIRE ITS USE.

Woman's AUXILIARY

Pima County Health Quiz. Photographed at new Tucson High School radio studio.

PUBLIC RELATIONS

Community service projects in Arizona have remained as diversified as ever in maintaining healthy Public Relations. However, there has been an added unity of purpose amongst the counties this year that has made the Public Relations program important in its scope.

In a statewide program the emphasis has been placed on public service through health education radio programs. A total of nine such programs under auxiliary sponsorship have emanated from seven different Arizona cities. When it is remembered that there are but seven organized counties, it is a remarkable record indeed.

All participating counties have used the excellent electrical transcriptions loaned by the American Medical Association's Bureau of Health Education. The amount of good accomplished by broadcasting any of the twenty-five different health series available from the A.M.A. is interesting. It becomes amazing when the ease of procuring radio time and the transcriptions is noted. The consensus is "why didn't we do it before?"

Why we didn't do it before is not so important as why we are doing it now and why we must continue.

The dissemination of health or medical information by the lay press has reached an all time high. The fact that some of this information is presented with bias is unfortunate to say the least. It is almost impossible to pick up a newspaper or popular magazine these days without finding a reference to medicine or health.

"Scare" articles, premature announcements of so called cures or miracle treatments, and the one in a million, medical oddity, have a guaranteed audience. Editors have found that the more sensational the material, the more avid the readership, and so we have a rash of articles telling the public "all."

The picture painted in consequence, is that the fine old gentleman known as our doctor is in reality, quite an ogre. They would have one believe that he is a money-grabbing, fee-splitting character, who performs all types of unnecessary surgery, (or has a "ghost" do it) and either hasn't had enough post graduate training, or on

the other hand, is too highly specialized. He never makes a night call, and it is just too bad that he doesn't know about the newest miracle drugs, or the dangers of the antibotics, unless of course, he too, has read the last issue of "Blurp."

What this type of article fails to mention is that many are written by advocates of socialized medicine and others by members of pressure groups. The whole effect has been that seeds of distrust have been sown and self diagnosis made by the now "informed" patient are quite common. The all too familiar, "Doctor, I have thus and so-itis and need a shot of Penicillin," even though thus and so-itis would never respond to treatment with Penicillin, is the type of thing that has been directly spawned by these so-called revealing articles.

To combat the situation, we have simply taken advantages of the fact that the public has shown a great interest in health facts. We supply them with authentic, health information, advocated by the A.M.A. Our various programs are not so flamboyant as the type with which we are competing, but are none the less effective in their good taste.

Each series is composed of thirteen, 15 minute electrical transcriptions, giving out information on everything from tuberculosis and cancer to baby care and alcoholism. The eight, A.M.A. series used in Arizona this year, total 104 programs. This should go a long way toward bringing some of the biased medical literature into proper prospective, and give the laity some helpful information.

The ninth radio program sponsored by an auxiliary, is Pima County's Health Quiz for school children. This is the same type of program inaugurated last year by the auxiliary in the Tucson schools. It has met with greater cooperation from both the school system and the radio station, and a possibility of televising the Quiz next year, has been mentioned. This twenty-nine week, 15-minute program has been a time consuming project, as is the production of any direct radio program. Pima is to be congratulated on its efforts.

There is a place for every county in this project, and for every city with a radio station, and just one interested doctor's wife. The transcriptions from the A.M.A. are loaned express prepaid, and are available for the asking.

The public wants health information and the radio stations are actually pleased to give time for public service features. It is only with an enlightened public, that better Public Relations can be realized. It is our business to see that the proper type of health education is made available.

Mrs. John K. Bennett
Public Relations Chairman
Tucson, Arizona

ARIZONA'S GUEST OF HONOR AT WORLD MEDICAL EVENT

Dr. Clara S. Webster, Tucson, Arizona

Dr. Clara S. Webster, Tucson physician, has been designated by Governor Howard Pyle to represent Arizona at the First Western Hemisphere Conference of the World Medical Association in Richmond, Va., April 23-25, 1953. Along with physicians from other states who are 75 years old this year, Dr. Webster will be honored by leaders of the medical societies of the United States and Latin America.

Medicine's greatest advances will be commemorated at the conference. Dr. Webster names as the five most important advances she has witnessed: asceptic surgery techniques, identification of various disease germs, new cheomtherapeutic drugs, improved anesthesia, and hormone therapy. She believes that the factors which have contributed most to increasing the length of life are "pediatrics, advance in medical education and geriatrics, and she adds, "The progress made in the entire field of medicine is so phenomenal that I have often felt happy to have lived to witness it."

A.M.A. Inaugural Ceremony Will Be Broadcast By ABC

The American Broadcasting Company Radio network will carry the inauguration of Dr. Edward J. McCormick of Toledo, Ohio, as President of the American Medical Association on Wednesday night, June 3, it has been announced by A.M.A. headquarters in Chicago.

The inaugural ceremony at the 102nd Annual Session of the A.M.A. in New York City will be heard over more than 300 ABC stations in this country, Alaska and Hawaii. Except for some local variations because of station program schedules, the inauguration will be carried at 10-10:30 p. m. in the Eastern Time Zone and 9-9:30 p. m. in all other time zones.

The actual inaugural ceremony will take place Tuesday night, June 2, in the Hotel Commodore, but it is expected that practically all radio and television time that night will be disrupted by special news and film programs on the coronation of Queen Elizabeth. It therefore will be necessary to transcribe the program for a delayed broadcast on Wednesday night.

Also originating from the A.M.A. New York meeting this year will be the popular "Dr. Christian" radio program, featuring the well known actor, Jean Hersholt. This program, which will be staged and transcribed Tuesday night one hour prior to the inaugural ceremony in the Grand Ballroom of the Hotel Commodore, also will be re-broadcast on Wednesday night. It will be carried by the Columbia Broadcasting System.

All physicians who will not be in New York for the A.M.A. meeting are urged to watch the radio listings in their newspapers for the local broadcasting times of the ABC inaugural program and the CBS "Dr. Christian" show, both on Wednesday night, June 3.

ROCKY MOUNTAIN CANCER CONFERENCE

The Seventh Annual Rocky Mountain Cancer Conference will be held in Denver on July 8 and 9. As in previous years there will be eight outstanding guest speakers, and on the first evening a banquet and entertainment for both the doctors and their ladies. There is no registration fee for this Conference.

PIMA COUNTY MEDICAL SOCIETY

James Malcolm Walsh, M.D., was elected to membership in the Pima County Medical Society on April 14, 1953. Dr. Walsh is engaged in general practice at the Phelps-Dodge Hospital in Ajo, Arizona.

Our speaker for the April meeting was Dr. James Barrett Brown, Professor of Clinical Surgery at Washington University School of Medicine in St. Louis. The subject of his talk was "Hemangiomas, Including Nevi," which was illustrated by lantern slides.

Robert B. Johnson, M. D., returned to civilian practice at 2430 E. Sixth Street, Tucson, on April 6th, after separation from the Armed Services.

Army Reviewing Physical Records Of 1,000 Priority 3 Physicians

The Army Surgeon General has asked area surgeons in the U. S. to review records of about 1,000 priority 3 physicians who were deferred for physical reasons prior to lowering of physical standards. A number of doctors in this group are expected to be found fit for duty. Under lowered standards announced last month, each case is decided on its own merits. Generally, the armed services are taking the position that if a doctor is physically able to carry on a private practice then he is fit for military service.

Since the Defense Department announcement on lowered standards, the Army has sent to Selective Service for re-evaluation the names of 739 deferred physicians in priorities 1 and 2. Of this group, 487 have received physical examinations.

A.M.A. Washington Letter

PATHOLOGICAL LABORATORIES—(Cont'd.)

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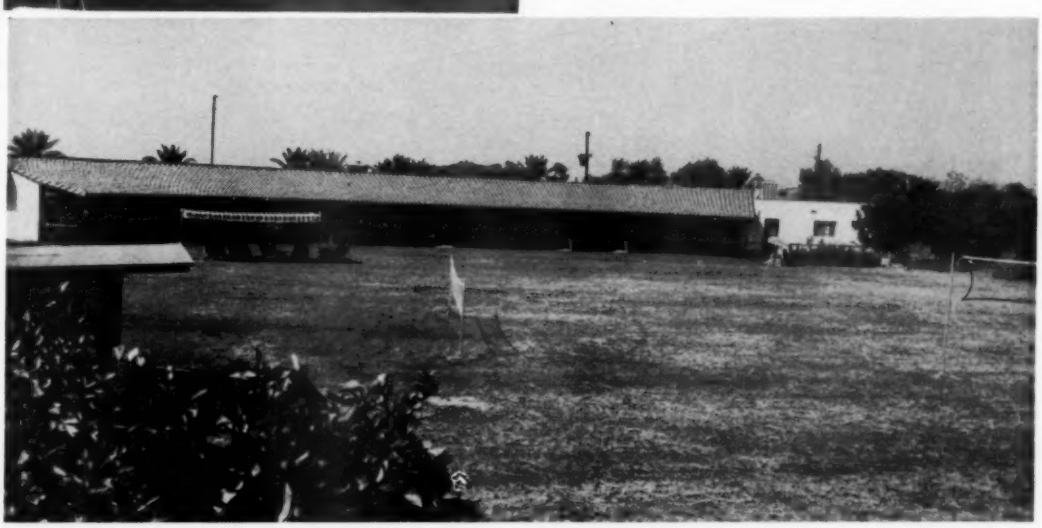

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